RADIOLOGY

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PRESENT STUDIES IN EXPERIMENTAL CANCER[1]

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ONE hundred thousand people die yearly of cancer in the United States. Every cancer worker, therefore, should pause and reflect whether the newer information gained in the clinic and laboratory within the past twenty years has brought about an increase in cures, or arrest of the disease. With this introduction, I hope to stimulate greater interest and better understanding of the present status of the cancer problem, and discuss with you in a general way some of the important knowledge gained from experimental laboratory studies, especially of the last three or four years.

For this purpose I have selected to touch only briefly upon the studies of experimental carcinogenesis, and a little more fully, perhaps, upon the biochemical mechanism of cell growth. Within the past two or three years research in cancer has narrowed down to practically new lines of investigation which have permitted a deeper insight into growth in general, and tumor growth especially. These studies, whilst at present incomplete, seem nevertheless to point in the right direction. Let me emphasize, for instance, the more recent production of artificial cancer without making use of the older technic of cancer tissue inoculation. Yamagiwa and Ichikawa (1) were the first to demonstrate that the repeated application of tar to the surface of the skin would finally induce cancer in mice. Tar or coal tar products are the foremost examples of chemical substances acting as irritants, and once malignancy has been induced artificially by these agents, the clinical, microscopical, and histo-pathological picture is identical with true carcinoma, or one that arises spontaneously. This work has been extended by Murray (2), Deelman (3), and Leitch (4), and a host of others, and has made possible detailed studies of the very earliest beginnings of neoplasia in the irritated areas. Cancer thus produced has enabled us to trace histological changes from the stage of chronic inflammation to the transitional stage, and finally into the state of a true carcinosis. Murray's (11) work especially deserves commendation, and special mention. He observed the interesting fact that a cancer produced in one area painted by tar will protect the animal from further development of irritation cancer, no matter how many areas are traumatized by the tar subsequently. Once the lesion has started in the deeper layers of the skin or in the stratum malpighii, it will continue to grow into a full-fledged carcinoma, even if the stimulus be left off. The artificially produced cancer continues to grow, invades adjacent tissue, forms metastases in the regional lymph glands, as well as in the internal organs, though the tar painting is further omitted. In this regard it resembles X-ray cancer. It is well known that, once malignant degeneration has

[1] Read before the Radiological Society of North America, June 5, 1924, at Chicago, Ill.

started, the withdrawal of the X-ray irritant does not inhibit or retard further progress of the cancer. The trend of all this leads to the assumption that the tar or X-ray irritant has produced something either in or around the cell. Whether this indefinite something has to do with inhibitory or stimulating effects upon the traumatized cells is as yet not clearly understood.

The significance of all this is, chronic trauma exerts a definite and specific action upon tissue cells. The importance of chronic irritation in the induction of new-growths is further augmented by the outstanding work of Drew (5, 8), at the Imperial Cancer Research Institute in London. Embryonic and tumor tissue, he states, when placed in suitable media, grow immediately, that is, within one or two days. Normal tissue of a young or adult animal, on the other hand, does not begin to grow *in vitro* until a lapse of ten to fourteen days. To illustrate: heart or kidney tissue in a suitable media lies dormant for ten to fourteen days, and then begins to grow. On the other hand, embryonic tissue or tumor tissue grows within one or two days under identical conditions. When, however, and this is the crux of the problem, kidney or heart tissue is damaged, the quiescent period is omitted, and growth takes place almost immediately. Therefore it seems not unreasonable to suppose that in the damaging of the heart or kidney tissue, something has been liberated which wipes out the latent period, and causes growth to take place immediately. This would indicate that under normal conditions the substance which stimulates growth immediately is either not elaborated in sufficient amounts, or is not present in an altogether free state. The nature of this substance is at present unknown, but earnest efforts are under way in quite a few laboratories to get nearer to its physical and chemical properties. There are quite a few notions as to the physiological part these substances play in nature, and to what extent they control normal growth and development. It has been possible to precipitate a growth-stimulating substance from serum by bubbling carbon dioxide through it (6). Shaking it for half an hour, or exposing it to 65 degrees C. for a few moments, destroys its activating power. Its activity diminishes if it is kept in the ice-box, and after two weeks the solution is entirely inactive. A decrease in the pH concentration of the media prevents its stimulating action. According to Carrel (6), it is quite sensitive to the action of radium and X-ray. Filtration through a Berkefeldt filter only partly deprives embryonic tissue juice of its growth-activating substance, though passage through a finer filter renders it entirely inactive. In the test tube the growth-promoting substance always remains with the protein precipitate.

The reason I have dwelt at length upon this phase of the growth-activating substance is quite obvious. It has been repeatedly emphasized by workers in this field that tumor tissue and also embryonic tissue are quite rich in this substance, in contrast to normal tissues in the young, as well as in the old. Carrel (6, 7) finds that fibroblasts grow and multiply only in the presence of extract of tumor tissue, or extract of embryonic tissue. It will be realized that these two extracts exhibit to the optimum the presence of a growth-stimulating substance. Nowhere else in the organism is this substance demonstrable in large enough amounts to aid tissue growth in artificial media. Drew also has made use of tumor extract or embryonal tissue extract as growth-stimulating substances in his tissue-growth experiments.

Carrel (9, 10), in addition, has demonstrated growth-inhibitory substances, through his studies of fibroblasts, that he has kept alive *in vitro* for the past eleven years. Serum, he points out, contains a growth-inhibitory substance. This inhibitory agent is present already in the serum of a six-weeks-old chick, and increases progressively in quantity with the age of the

fowl. The restraining action of serum can be increased by the action of radium and X-ray. Let us pause here for a moment to consider the importance of increasing the inhibitory substance by radiation. If this increase of the inhibitory power can be effected by X-ray and radium, it seems to argue that we are on the right track in utilizing these agents in the treatment of cancer.

To put this in a more compact form, let me recapitulate: Tumor and embryonal tissues are particularly rich in a substance which activates cell proliferation. Serum, on the other hand, demonstrates an inhibitory substance. Thus we have here exemplified two diametrically opposed substances, the one growth-stimulating, the other growth-inhibiting. In the present state of our knowledge it is held that both substances are in equilibrium in the organism throughout life, their action, however, masked by the counteraction of one upon the other. Further, traumatism, be it external or internal, may cause by repeated processes of constant repair, a disturbance of the normal equilibrium of these two substances. Hence, two possibilities come into question, either an excess of growth-promoting substance giving rise to increased cell proliferation, or an enhanced depressing effect causing inhibition of cell repair. This seems to be borne out in particular in the production of experimental tar cancer. Although a large area of skin surface is traumatized for several months, the transition from a chronic ulcer into a cancerous growth is confined to a strictly localized area of a few cells. Once it has started in this minute area, there is no checking it, even if the traumatic agent is withdrawn. To quote Murray: "From these observations, many times repeated, and always with the same result, it is concluded that these malignant growths produce continuously, of their own accord, growth-stimulating substances which normal cells elaborate only in response to cell damage, and when, by constant repetition, this production has become automatic, proliferation will continue after removal of the initial cause of the protoplasmic disintegration. Temporary hypertrophies would, in this conception, correspond to the purely reactive production of activator, ceasing when the irritant is removed; benign growth to an autonomous production in small amounts; and malignant growth to more abundant production." You will agree that this side of the cancer problem offers perhaps the most attractive and hopeful outlook, and more work along these lines within the near future will open up new facts, and lead to greater promise.

No scientific paper on neoplasms seems complete without at least a brief discussion of heredity. The studies in cancer heredity have been elaborated most admirably by the extensive experimental work of our foremost biologists. The names of Morgan, Davenport, Little and Slye are almost laboratory by-words in heredity. It has not been possible to correlate these ingenious laboratory experimentations with clinical manifestations. According to Little (15), many more factors aside from the recessive and dominant characters isolated through inbreeding are essential to complete the chain of heredity. On the other hand, it is difficult to discount the experiments upon tumor incidence carried out upon the largest scale by Dr. Slye (23). As you know, her work dates back over twelve years, and more than 40,000 mice have been autopsied, and a great deal of valuable information obtained. Clinically the ability to resist or develop the disease depends upon many other factors. Quite aside from hereditary influences chronic irritation, for instance, cannot be ignored, especially, as I have mentioned before, that experimental tarring will eventually induce cancer in practically 100 per cent of animals. In addition, it is well known that the inoculation of a virulent tumor will result in 90 to 100 per cent takes, notwithstanding dominant or recessive factors. There are too many instances of cancer

arising from definite traumatizing agents, as the gastric cancers in Fibiger's (12) experiments, produced by feeding rats with roaches infested with the intestinal parasite, spiroptera neoplastica. So, too, the Crocker Research Laboratory (13) reports that malignant degeneration of liver cysts can be produced at will when rats are fed with the eggs of the tapeworm of the cat. In this connection the crown gall cancers of plants warrant consideration. Erwin Smith (14) finds that chemical irritants from the specific Bacterium Tumefaciens are capable of initiating malignant new-growths in plants. There is little use of pointing to other forms of irritating cancer, as X-ray, paraffin, aniline dyes, and so on. The many investigations of human cancer families leaves a great gap to be filled in by future studies, as at present all work in heredity, experimental as well as clinical, has failed to offer any practical assistance in the control of susceptibility or resistance to cancer. Clinically we see both parents succumb to cancer, and still the offspring may be free of the disease. All in all the entire subject of heredity in human cancer seems too complex and involved at present to permit of drawing any definite conclusions.

In like manner the experimental work in immunity to cancer has held our renewed interest within the past few years. The work of Murphy (16) and his collaborators concerning the rôle of the lymphocyte in immunity unfortunately has been counteracted by the destructive evidence of my own (17) experiments, corroborated by those of Prime and Wood, Kellert and others. Little aid can be expected from the artificial stimulation or destruction of lymphocytes in the fight against cancer. In my own work (18) it has not been possible to break down a natural immunity by the destruction of lymphocytes. This was clearly demonstrated by the administration of intensive radiation to immune animals, causing almost complete depletion of lymphocytes. When animals in this lymphopenic state were inoculated with cancer grafts, no difference in their refractory behavior was discernible. On the other hand, susceptible animals could not be made immune by any manner of hyperlymphocytosis. The injection of leukocytic cream of radiated animals, rich in lymphocytes, produces a high degree of lymphocytosis in a normal animal. Notwithstanding this hyperlymphocytosis, the animals behaved to tumor growth exactly like those that did not receive this super-imposed lymphocytic extract. These negative experimental findings are borne out by our clinical studies, where we frequently encounter a relatively high percentage of lymphocytes in many cancer patients. In this connection the work of Chambers and Russ (19, 20), at the Middlesex Hospital in London, is interesting and important enough to merit consideration. Contamin, Wedd, and Russ (21, 22) first drew attention to the immunizing effect of injections of radiated tumor tissue into normal animals. With the determination of the lethal dose for cancer tissue, Chambers and Russ extended these studies into the clinical field. Sterile tumor tissue removed at operation was aseptically radiated with a lethal dose. This radiated emulsion was injected subcutaneously into the abdominal wall with the hope of conferring immunity and preventing recurrences of metastases. In a personal communication to the author, very striking results were reported three years ago. At the present time, however, the final value of this drastic procedure has not been encouraging, as further corroborating reports are wanting. To complete this brief review mention must be made of a striking piece of research that has come to our notice from a Japanese observer. All former research in animal cancer has demonstrated a "species specificity." In other words, a tumor of the rat would grow only in another rat, one of the mouse in another mouse, and all attempts at zigzag transplantation from mouse to rat or rat to mouse, etc., had failed. Shirai (24), how-

ever, demonstrated the possibility of inoculating a rat tumor into the brain of a mouse, or pigeon, or guinea pig, whereas a subcutaneous inoculation fails to grow. This has upset all our former notions, and opens up a new line of investigation. Analyzing all these newer studies in immunity to cancer: Whilst they are very interesting and have brought new facts to bear upon the problem, nevertheless they lack at present a clear-cut basic formula.

Space will not allow more than the merest mention of the newer experimental studies of radiation in cancer. I must resist the temptation to trace in detail the progress in this field within the past four years, as the work on this subject is quite familiar to everyone here. The conclusions arrived at during the recent Radiological Congress in Berlin at the end of April, this year, deplore the lack of biological explanation concerning the dispersion and absorption of radiant energy in the tissues.

In this brief survey of experimental cancer, I have by no means enumerated all the investigations which bear upon this great problem, and the discussion of many important observations naturally had to be curtailed. If in the main the important questions about carcinogenesis are still unanswered, it is because we are still ignorant of many factors which control normal growth and development. It is desirable, therefore, that we have more precise knowledge of the stimulating and inhibitory basis regarding growth in general, in order to correlate it with the normal repair of tissues, and with the changes into malignant proliferation. The admirable work in this direction within the past two or three years has brought to light definite and undeniable proof that a long-continued irritation will cause traumatized tissues to throw off normal restraint, finally to succumb to lawless and unrestrained new-growth.

The problem that confronts us is how to prevent malignant transformation of a normal cell, and once the malignant transformation has set in, how to destroy the cell. If by some means we can also determine accurate quantitative measurements of the activating and depressor substances of different cellular elements and body fluids, we may then at least feel that our feet are firmly set on the road to fuller knowledge, in order to approach and reach the nucleus of the entire cancer problem.

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Colonic diverticula.—Colonic diverticula occur most frequently in individuals past forty years of age. Statistics show that males are affected two or three times as often as females. The typical patient is rather obese, not anemic, and apparently not very sick.

From the pathological standpoint colonic diverticula are, when not congenital, practically always of the "false" type. They consist of a herniation of the mucosa through the muscularis; while on the outer surface of the bowel, if the situation permits, there is often a patch of adhesive peritonitis. The number varies in each case from one to three or four hundred. They are most commonly found in the sigmoid and descending colon but are not infrequent in the rectum and may occur in the cecum and transverse colon. Their most common location is at the ante-mesenteric border. When not accompanied by an inflammatory process the condition should be referred to as "diverticulosis;" when inflammation is present it becomes "diverticulitis."

The roentgen-ray appearance of these cases is very characteristic. There is, however, some difficulty in bringing out the typical appearance on the films or under the roentgenoscopic screen. These pockets being already filled with fecal matter, do not readily outline with the barium mixture and the first examination, even in a case with numerous well-marked diverticula, may show no filled pockets. In such cases, however, the involved portion of the bowel nearly always presents a ragged, spastic appearance, which, while not characteristic, is suggestive and should lead to further study. Barium pent up in contracted haustra may occasionally resemble diverticula, but manipulation during screen examination and particularly a series of films after the meal and after the enema will serve to differentiate this from true diverticula.

The ideal sequence for confirming a diagnosis of diverticulitis consists in visualizing the filled pockets after the barium meal, allowing the colon to empty until only the filled diverticula are shown on a 48- or 72-hour film, and then demonstrating them as extra-luminal shadows after the enema.

J. D. CAMP, M.D.

Diverticulosis and Diverticulitis of the Colon. C. D. Enfield. Am. Jour. Roentgenol. and Rad. Ther., Sept., 1924, p. 242.

Principles of cancer therapy.—At a discussion of cancer therapy during a meeting of the Royal Society of Medicine, in March of 1924, the keynote of most of the remarks was a disappointment with the results obtained since the introduction into England in 1921 of X-rays generated at 200,000 to 230,000 volts. Many speakers frankly stated that the new methods were, in their opinion, no better than the old. The writer himself has been unable to discover any difference in the results in pelvic cancer,—the same temporary miracles being accomplished in both cases. In breast cases, he believes that the longer wave length had a rather better effect.

His conclusions are:

1. The wave length most suitable for any given type of growth can be found only by clinical observation.
2. Malignant tumors should be regarded from a dynamic and not from a static viewpoint. The microscope does not enable one to say that any two tumors are really alike.
3. The still healthy parts in the neighborhood of a tumor play a vital part in the success of any therapeutic measure.
4. When "intensive dosage" is used, the amount of radiation which is concentrated upon a tumor should not exceed the maximum consistent with the production of a healthy reaction in the surrounding tissues.
5. The intensive method should rarely be used to render a case operable, and never as a prophylactic after operation. For this purpose the small divided dose is alone suitable.
6. If an injury is inflicted by rays of a given wave length, the lesion may be cured or mitigated by rays of a widely different wave length.

SOLOMON FINEMAN, M.D.

Some Principles of Treatment in the Radiotherapeutics of Cancer. Francis Hernaman-Johnson. Lancet, Sept. 27, 1924, p. 635.

THE FUNDAMENTAL HARMONY SHOWN IN ALL ESSENTIALS IN SPONTANEOUS NEOPLASMS AND IN TRUE EXPERIMENTAL TUMORS[1]

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THE intensive study of any medical problem along many widely divergent lines is likely to bring out a mass of facts which may seem somewhat antagonistic, when viewed superficially. Such a situation has arisen at the present time in the field of cancer research, and there is, therefore, a need for synthetic consideration of these apparently divergent facts, which are divergent in appearance only.

It is the aim of this paper to give such synthetic consideration to two of these apparently divergent facts, brought out by cancer research, and to suggest some of the missing links. I refer to the behavior of spontaneous newgrowths, and to that of experimentally produced tumors in some of their apparent differences, as shown in laboratory studies of both types of animal neoplasms.

I shall take as the main criterion of comparison, the inheritance behavior of the various types of tumor production, since the inheritance behavior of any organic character or entity is its biologic fundamental. As I pointed out in a preceding article[2], the whole process of organic development represents the unbroken functioning of heredity in each minute and infinitely interrelated detail, transmitting types of protoplasmic behavior from ancestor to offspring. So infinitely interrelated are the minutiæ of organic life, that their behavior in heredity is very difficult of complete analysis. The ready conclusion, therefore, is frequently drawn that heredity does not underlie the behavior of all minutiæ of organic life, because it is not always superficially apparent.

The logic of the matter is certainly evident: similar tissues must function in the same way unless they are forcibly prevented from doing so, because they were derived from a common ancestry with only a given type of possible behavior. That they can be forcibly prevented from doing so is no more to be disputed than that an infant's leg can be cut off and prevented from growing to the inherited length.

Let us consider in sequence the various types of artificially produced tumors and compare them with spontaneous neoplasms in some of their biologic fundamentals.

I. TUMOR CELLS GROWING IN VITRO

When living tumor cells are placed in a test tube or other mechanical container and are given the right conditions of attachment and food[3] they perform the common inherited function of all nourished living cells, that is, they divide and the mass grows. We have here the neoplasm reduced to its lowest terms, and manifesting the only inherited behavior types possible in its restricted location, namely, the absorption of food and the undifferentiated mass growth by cell division, sarcoma cells producing undifferentiated sarcoma only and carcinoma producing undifferentiated carcinoma.

There is nothing for the tumor to infiltrate into, and no organ for it to invade by metastasis. It merely grows according to its type, up to the limits set by its environment. Its cell division and mass growth are potentialities inherited from the original spontaneous tumor of which it was a part, and mean nothing with reference to the inheritance possibilities of its artificial host. If the food is withdrawn, the tumor

[1] Read before the Radiological Society of North American, at Chicago, June, 1924.

[2] Biologic Evidence for the Inheritability of Cancer in Man. Jour. Can. Res.. VII, No. 2, 1922, p. 107.

[3] Lambert and Hanes, Jour. Exp. Med., XIV, 1911, p. 129.

cells cease dividing, and die. It thus manifests another type of inherited behavior of protoplasm. Its cessation of cell division and its death mean nothing with reference to inherited possibilities of the test tube. They are concerned only with the tumor cells.

II. GRAFTED TUMORS

When living tumor cells are grafted into a living host, and are given the right conditions of attachment and food, they also perform the common inherited function of all nourished living cells, that is, they divide and the mass grows. We have here a more complex problem of inheritance behavior than that furnished by the tumor cells growing *in vitro*. The behavior problem is now two-fold: the inheritance behavior of the piece of tumor and the inheritance behavior of the living container into which it has been grafted.

The tumor tissue grafted into the living host manifests exactly the same fundamental types of inherited behavior shown by the tumor cells growing *in vitro*, namely, absorption of food with consequent cell division and mass growth; and cessation of cell division, with consequent death, when nutriment is withdrawn. Its cell division and mass growth and its death if nutriment is withdrawn, mean nothing with reference to the inheritance possibilities of the living host into which the tumor has been grafted. Its inheritance potentialities are those of the tissues of the animal of which it was a spontaneous tumor, not those of the tissues of its host. Here, also, as in the case of the tumor cells growing in the test tube, the cell mass, when given proper conditions of attachment and food, grows without differentiation and without control up to the limits set by its environment.

The environment of the grafted tumor, however, instead of being a mechanical container, is a living organism with inheritance potentialities of its own, which must determine the limits set for the growth of the parasitic tumor, but not the fact or the type of the growth itself. If the host normally regenerates its own cells, assaulted by the inoculation, and builds up an accessory circulatory system for the graft so that nutriment is supplied, the cells of the parasitic tumor continue their division and mass growth. If the adjacent tissues of the host do not regenerate and do not build up an accessory circulatory system, no nutriment is furnished the parasitic cells, that is, they are not given proper conditions of attachment and food, and consequent cell death occurs, with the sloughing out of the graft. That is, we do not get "a take." "A take" of grafted tumor fundamentally, then, depends upon the *normal regeneration* of the assaulted tissues, and not upon the abnormal growth of the host cells.

Following the demonstrations by Loeb and by Jensen, about 1900, showing the possibility of inoculating rat and mouse tumors, a great deal of work was done with such tumors, much of which concerned itself with the problem of the inheritability of cancer, notably the work of Tyzzer[4] [5] and later of Little and Tyzzer[6].

Since the beginning in this laboratory, of studies in the inheritability of spontaneous neoplasms, in 1910, the fundamental differences between spontaneous and grafted tumors have been made increasingly apparent[7]. No further evidence of the intrinsic difference between spontaneous and grafted tumors is needed than Tyzzer's own results in later obtaining spontaneous tumors in individuals that had refused grafts[8]. Bashford also reported that animals immune to inoculation were capable of developing spontaneous tumors[9], and others have made similar observations.

There undoubtedly is an interesting inheritance problem in these genetic studies carried on with transplanted tumors. It concerns itself, however, with the inheritability of tendencies of the assaulted tissues to regenerate normally and to build up an

[4] Jour. Med. Res., XVI, 1909, p. 519.
[5] Jour. Can. Res., I, 1916, p. 125.
[6] Jour. Can. Res., VI, 1921, p. 106.
[7] Jour. Can. Res., V, 1920, p. 72.
[8] Jour. Med. Res., XVI, 1909, p. 479.
[9] Fourth Sci. Rep., Imp. Can. Res. Fund, XIX, 1911.

accessory circulatory system, and not with the inheritability of the tendency to regenerate abnormally, as is the case in cancer. A very large field of metabolic behavior is opened by these genetic studies of grafted tumors, but the inheritability of spontaneous cancer, and many other problems of spontaneous cancer behavior, do not lie within the field of grafted tumor studies.

Let us apply here the criterion of inheritance behavior between these grafted tumors and spontaneous animal tumors. Little and Tyzzer, who carried out the most extensive and conclusive of these genetic studies of grafted tumors, found that heredity controls the susceptibility to these tumors in various strains of mice, but that susceptibility and non-susceptibility do not behave as unit characters, but rather as a complex of unit characters, probably many in number. Susceptibility to these grafted tumors uniformly appeared in the first hybrid generation in 100 per cent of the cases, and in steadily decreasing frequency in later generations.

The appearance of susceptibility to grafted tumors in the first hybrid generation between pure stocks, would show that one of the most important factors concerned in the transmission of susceptibility to grafted tumors must be a dominant. The logic of the situation confirms this conclusion, for obviously the first and most important factor in determining the acceptance of a graft, whether of tumor, of bone, of skin, or of any other organic tissue, is the ability of the assaulted tissues to regenerate normally, and thus to give proper conditions of attachment and food. Obviously, if the tendency to regenerate abnormally, as in cancer, were dominant over the tendency to regenerate normally, very little would remain in the organic world but cancerous individuals.

Similar inoculation experiments carried out on mice by Loeb and Fleisher[10], although differing in details, agreed with Little and Tyzzer's work in essentials, that is, susceptibility to the implant occurred in the first hybrid generation, showing the presence of a dominant concerned in the susceptibility; and the method of inheritance in later generations indicated a multiple factor. Obviously, since the tendency to regenerate normally is dominant over the tendency to regenerate abnormally, all genetic studies with grafted tumors, must, if the technic is accurate, show susceptibility to inoculation in the first hybrid generation of susceptible strains.

The fundamental basis of susceptibility to grafts, then, is the exact opposite of the fundamental basis of susceptibility to spontaneous cancer, which is the tendency of the assaulted tissues to regenerate abnormally in the uncontrolled and undifferentiated method of the neoplasm.

III. SPONTANEOUS TUMORS

Prior to the year 1910 most of the work in cancer research had been done with grafted tumors. The relative ease with which this grafted material was procured, and the extreme difficulty of securing a stock of animals with spontaneous cancer, naturally led to the selection by practically all workers of the easily secured material. As has already been pointed out, a grafted tumor is in the nature of a parasite growing in a foreign host. It is the cells of the graft that proliferate, not the cells of the host. A spontaneous neoplasm is the result of the cell proliferation of the tissues of the animal itself, and is the outcome of its own metabolism. Its fundamental biology, therefore, must in all its ramifications be different from that of a grafted tumor.

The material used for the studies carried on in this laboratory has been fully described in previous publications.

As the results of this work have been serially published for the last ten years, with masses of exact data and genealogical charts[11], I shall only summarize certain of those results here.

[10]Cent. f. Bakt. u. Parisit., LXVII, 1912, p. 135.

[11]Jour. Can. Res., VII, 1922, p. 146.

Inheritance of Spontaneous Neoplasms

The inheritance behavior of spontaneous neoplasms is opposite from that of grafted tumors. Contrary to the behavior of grafted tumors in heredity, which has been shown to involve multiple factors, the main factor being a dominant or the ability of the assaulted tissues to regenerate normally, the inheritance behavior of spontaneous cancer has uniformly been that of a simple Mendelian recessive, throughout the entire results obtained in this laboratory. The immediate basis of spontaneous tumors is the tendency of the tissues to regenerate abnormally to assaults of various kinds, that is, to chronic or acute irritations, and this tendency to regenerate abnormally has uniformly behaved like a recessive unit character, in matings between pure cancerous and pure non-cancerous individuals.

Throughout the hundreds of matings made in this laboratory, between analyzed cancerous and non-cancerous mice, the cancer tendency has never in a single instance appeared in the first hybrid generation. This shows conclusively that susceptibility to spontaneous cancer cannot be dominant over resistance to cancer. Here, in this basic difference between susceptibility to grafted tumors and susceptibility to spontaneous cancer, we have the explanation of the different results obtained by students of cancer heredity working with grafts, and those working with spontaneous neoplasms. In both types of studies the tendency to regenerate normally has uniformly been shown to be dominant over the tendency to regenerate abnormally.

IV. EXPERIMENTAL LIVER SARCOMA IN RATS

There is now under way in the Crocker Research Fund laboratory, the experimental production of liver sarcoma in rats, by the feeding of the larval stage of the tapeworm of the cat. Bullock and Curtis[12] in 1920 reported as follows:

There were 1,165 original rats fed with a suspension of tapeworm eggs, 10 to 60 eggs to the drop, one or two drops being given each rat. Six hundred rats were killed five months after feeding, none of them showing any tumor. Five hundred sixty-five of these experimental rats then remained alive. Of these 565 rats, 230 were killed or dead fifteen months after the original feeding. Fifty-five of them showed liver sarcoma, *i.e.*, 510 of them did not develop liver sarcoma in fifteen months.

Twenty-five hundred descendants of the original rats were added to the experiment, making a total of 3,665. Thirty of the first generation descendants also showed liver tumor, making a total of 85 that had liver sarcoma out of 3,665 rats fed with tapeworm eggs. Thirty-five hundred eighty, then, of the rats thus fed did not develop liver sarcoma.

The authors state that young rats of certain strains seemed most likely to produce these experimental liver tumors. They further state that most of the tumors undoubtedly arose in the walls of parasitic cysts, and that the others were probably of the same origin. The authors do not state whether tapeworms were found elsewhere than in the liver in larval stage. None of these rats is reported to have shown tumors in any other location except in the liver and regional metastases. They state that certain strains are more susceptible than others, and at the 1923 meeting of the American Association for Cancer Research, Wood reported that when rats that developed liver sarcoma were bred together, much higher rates were obtained in the offspring, such families sometimes giving 100 per cent of positive results. This shows a most striking hereditary basis underlying the success of this experiment.

It is of interest also to note, that, in an article concerning "a transplantable myosarcoma" of the rat[13], Bullock and Curtis report a spontaneous tumor of this type

[12] Proc. New York Path. Soc., XX, 1920, pp. 6-8.

[13] Jour. Can. Res., VII, 1922.

occurring in the tail of a rat which had been infested with tapeworm larvæ without developing a liver sarcoma, thus showing that this rat developed the type of tumor to which it was predisposed rather than the type of tumor experimentally attempted.

V. PATHOLOGIC CONDITIONS RESULTING FROM NATURALLY INGESTED TAPEWORM

Every effort has constantly been made in this laboratory to exterminate all vermin and parasites, such as lice, flies, bedbugs, cockroaches, tapeworms and nematodes, and the more perfectly these parasites are eliminated, the higher is the spontaneous tumor rate. In spite of these constant efforts there have been periods when the stock has shown both tapeworms and nematodes, notably when local tramp house mice and wild Norway rats have been carrying the same types of parasitic worms.

Among the 43,984 autopsies performed in this laboratory to date, there have been 1,600 cases of tapeworm naturally ingested. Among these 1,600 mice with tapeworm, there have been 157 with tumors, leukemia or pseudo-leukemia. The tumors in mice with both tapeworm and neoplasms were distributed as shown in the tabulation on this page.

There is no reason to suppose that the four liver adenomas were caused by tapeworm any more than the other 165 neoplasms in infested mice, since in three of the cases there was no worm cyst in the liver, adult worms being in the intestine and common bile duct; while in the single case of liver adenoma where there was a liver cyst, the walls of this cyst showed no proliferation whatever, and the adenoma was in a different lobe of the liver with no cyst in that lobe.

On the negative side the evidence is still more striking. There were 1,695 cases of liver parasites that did not produce liver tumor even in strains which normally produce 50 per cent liver tumor incidence. The mice in these 50 per cent liver tumor

Mammary gland	101	95 carcinomas 3 sarcomas 3 adenomas
Lungs	32	adenomas and adeno-carcinomas
Liver	4	adenomas {3 had no worm cyst in liver 1 had no adjacent cyst in liver
Ovary	1	adenoma
Prostate	1	sarcoma
Preputial gland	1	adenoma
Testicle	2	{1 carcinoma of 6 nodules 1 mesothelioma
Jaw	3	squamous cell carcinomas
Thymus	2	lymphosarcomas
Retroperitoneal tissues	1	lymphosarcoma
Spinal column	1	myeloma
Stomach	1	sarcoma
Mouth	1	sarcoma (at site of wound)
Eyelids	1	squamous cell carcinoma
Leg	1	osteosarcoma (point of fracture)
Hip bone	1	osteosarcoma (point of fracture)
Pancreas	1	carcinoma
Duodenum	1	carcinoma
Head	1	squamous cell carcinoma
Total	157	
Leukemia	5	
Pseudo-leukemia	7	
Grand total	169	tumors, leukemia and pseudo-leukemia

strains which had liver tumor did not have tapeworm, and the mice in these strains that had tapeworm did not have liver tumors.

Only 157 of about 5,000 spontaneous neoplasms in this stock were in mice infested with tapeworm. That is, about 97 per cent of these neoplasms occurred in mice not infested, making it beyond dispute that the origin of neoplasms is in no way dependent upon the presence of tapeworm.

There is a perfectly standard result of the normal ingestion of tapeworm, as shown by autopsies in this laboratory, and it does not involve neoplastic proliferation in the liver or elsewhere either in the mice of tumor strains or in mice of non-tumor strains, but, instead, the results are of a highly degenerative character.

It is interesting also to note that the wild house mice, the wild Norway rats and the albino rats autopsied in this laboratory, which have had tapeworm, have shown exactly the same types of pathologic changes shown by the mice in this laboratory.

As stated in a previous article[14], complicating diseases such as tapeworms and nematodes in the digestive tract or any other highly destructive disease, greatly retard spontaneous tumor growth. For example, if we compare tumorous mice (after they have ceased reproducing), these mice all being from the same or allied strains and of about the same age, we get some interesting facts. We find that mice without tapeworm, nematodes or any other highly destructive disease, grow on an average nearly twenty-five times as much tumor daily as do mice infested with tapeworms or other highly destructive parasites. In the experience of this laboratory, then, instead of causing tumor growth in the liver or elsewhere, the infestation of mice by tapeworms or nematodes, etc., greatly retards the growth of such tumors as the animal develops.

The difference between the pathologic findings in the Bullock and Curtis experiment of artificial feeding with tapeworm eggs, and those in this laboratory from normally ingested tapeworm, are certainly striking. Whereas they report a considerable percentage of liver sarcomas arising in the walls of cysts containing live tapeworm larvæ, and do not report any degenerative changes, as the result of this feeding, the findings in this laboratory are exactly opposite, namely, no liver sarcomas or other neoplasms traceable in any way to tapeworm larvæ, no proliferation of any sort in the cyst walls containing either living or dead larvæ, and the most extensive degenerative changes causing death, as the result of naturally ingested tapeworm eggs. Moreover, 122 of the total 126 liver tumors arose in mice which had no tapeworm or any other discoverable parasite.

There are two suggestions which may throw some light upon these apparently widely divergent results from the ingestion of tapeworm eggs: (1) Bullock and Curtis evidently did not make any biologic analysis of the stocks used in their experiment, in order to determine what percentage of these rats would produce liver tumor without the ingestion of tapeworm eggs. That there was a biologic difference in the various strains in the matter of tumor production, is shown by the different percentages of tumors arising in the different strains used, and also the difference in the formation of lung metastases among the different strains. (2) If we assume that all of these liver sarcomas in rats were due only to the irritation of tapeworm larvæ upon the walls of the cysts, there remains a synthetic suggestion which will correlate their results and mine.

Bullock and Curtis state that all the tumor-bearing rats presented multiple cysts in the liver, varying from 6 to 84 in number. Obviously the rats whose livers contained 84 larval cysts must have swallowed at least 84 eggs. No mouse has ever been found in this laboratory with more than five tapeworms or larvæ. The relatively

[14]Jour. Can. Res., V, 1920, p. 5.

few tapeworm eggs normally ingested by mice in this laboratory or by the wild rats and wild house mice which I have autopsied, apparently did not produce an irritating effect of the type to overthrow their normal regenerative powers in the tissues of the liver, even in the strains subject to 50 per cent of spontaneous liver neoplasms, but instead, produced a violent effect sufficient to cause fatal degenerative changes, with no opportunity for proliferation of any sort.

Whereas, the 60 to 84 experimentally fed tapeworm eggs (assuming that the irritation from the larvæ was in every case the certain cause of the proliferation) apparently were efficient in producing an irritation in 85 rats capable of overthrowing their normal regenerative powers in the tissues of the liver, and not sufficient to cause fatal degenerative changes. It is, however, difficult to see why, as Bullock and Curtis state, only one of these cysts usually showed proliferation, if the irritation of the cyst content was the efficient cause.

Even if it should prove to be possible to cause liver sarcoma in every animal by the ingestion of tapeworm eggs, this would not disprove the inheritability of cancer—for note the biologic facts.

There resides in every living organism the power to regenerate within certain limits. These limits are set by the normal metabolism of the organism. For example, under normal conditions a beheaded planarian can regenerate a head. But if this beheaded worm is put into a solution of alcohol, not lethal in strength, it is no longer able to regenerate a head, but will perform partial regeneration in proportion to the strength of the alcohol solution. If the solution is sufficiently strong, all power of regeneration is lost.

If sea urchin eggs are centrifuged, they will not generate normally. If the centrifuging is sufficient, they will not generate at all. A less degree of centrifuging will produce abnormalities of generation, proportionate to the degree of centrifuging used.

These facts demonstrate that it is possible to overthrow partially and even completely, not only the normal inherited regenerative powers in the tissues of an organism, but even the normal inherited generative powers. There is no organic mechanism which cannot be overthrown wholly or in part, by a sufficiently strong assault. For example, it is possible by a sufficient assault, to destroy the pigment-making mechanism in a young mouse with inherited black hair, and thus cause local albinism at the point of assault. But this fact has nothing to do with the inherited pigment-making function or its potentialities under normal conditions.

A parallelism to these facts of normal regeneration and generation, and the possibility of their destruction, partial or complete, undoubtedly exists in the facts of abnormal regeneration operating in the production of neoplasms. Resistance to neoplasms has consistently behaved like the presence of a mechanism fitted to control proliferation and differentiation in regenerative processes. This mechanism, like the pigment-making mechanism, it is undoubtedly possible to kill; so that by an efficient assault it might be possible to produce a local lack of this mechanism, just as we can produce local albinism by an assault upon the local and inherited pigment-making mechanism.

Again: the pigment-making mechanism exists in different degrees among different individuals, so that among mice, for example, some individuals form red pigment (most highly oxidized melanin); some individuals form gray pigment (a less degree of oxidation of melanin); some individuals form black pigment (a still less highly oxidized melanin); and so on, down to those individuals whose pigment-making mechanism is of the type which produces only the palest blue or cream color, the latter being barely distinguishable from albinic white.

In just this way, individuals may vary greatly in the degree of their mechanism for controlling growth and differentiation

in regenerative processes, *i.e.*, the cancer-resistant mechanism. Individuals of the first class, who have the highest degree of non-cancer mechanism, would then rarely produce cancer under any provocation, but individuals with the lowest degree of cancer-resistant mechanism might relatively easily succumb to artificial conditions for cancer production. Whereas under the normal life of the organism, no set of circumstances would arise that could produce cancer, under the continued and artificially excessive provocation it might succumb; just as an individual with enormous muscular power, capable of resisting any normal impact against his musculature, would succumb under the impact of 100 tons. His mechanism, efficient under normal conditions, would have no opportunity to function. Many of the experimental procedures using artificial means of producing tumors may easily be of this shattering type. So that, in those individuals that have only a low degree of cancer-resistant mechanism, this controlling mechanism may have no opportunity to function.

However, none of the stocks used for the experimental production of cancer, so far reported, has ever been analyzed as to its natural cancer potentiality, and therefore we have no scientific basis for decision as to what part of the results of such experiments is due to natural cancer potentiality and what portion remains the unquestioned experimental result.

It might then be possible, by a violence sufficient to destroy the cancer-resistant mechanism, to cause cancer in every organism, the readiness with which this could be done being dependent upon the degree of cancer-resistant mechanism possessed by each individual.

It may, therefore, be possible to discover a type or types of irritation sufficient to cause neoplasms in every living organism; and tapeworm larvæ, nematodes, coal tar painting and X-ray burns, along with other types of irritation, may any or all of them prove to be efficient causes for the overthrow of inherited cancer-resistant mechanism, just as all heads can be turned gray or even cut off, no matter what the inherited potentialities might be; for one inherited potentiality of every organic mechanism is that it can be destroyed by some form of assault. The inherited mechanism for cancer resistance, therefore, would not differ in this respect from every other inherited potentiality; that is, it undoubtedly can be destroyed.

The reverse also may prove to be possible. Susceptibility to cancer has consistently behaved like the absence of a mechanism fitted to control proliferation and differentiation in regenerative processes. If this absence should prove to be systemic it might be possible so to stimulate the defective center as to cause it to function at least with partial efficiency, as a defective pancreas can be fed with insulin. If the defective mechanism should prove to be local, it might prove to be possible to implant a local mechanism, either physical or chemical.

Biologically, therefore, cancer therapy must be one of two sorts: either the removal or destruction by surgery, radium, X-ray or other destructive agents, of the local tissues lacking the mechanism for resistance, or the finding of a defective local or systemic center for resistance to cancer which by artificial stimulation can be made to function efficiently, at least temporarily, in the control of regeneration. The heredity behavior of cancer, however, has consistently been that of a local lack of mechanism, since susceptibility to tumors of specific tissue in specific organs is inheritable, and strains of mice never showing mammary gland carcinoma, produce 100 per cent lung tumors, etc. This fact argues a local rather than a systemic lack of mechanism.

VI. THE ARTIFICIAL PRODUCTION OF SPIROPTERA CARCINOMA IN RATS AND MICE

Fibiger states that he produced 54 squamous cell carcinomas in the digestive tract[15]

[15] Det. Kgl. Dan. Vid. Sel. Biol. Med., 1918, p. 17.

in 116 rats fed with nematode larvæ. Also in experiments, possibly still under way, he had at the time of publication observed three cases of carcinoma in the fundus of the stomach of white mice[16] fed in exactly the same way upon these larvæ.

Fibiger's reports show (1) that there is a difference in susceptibility among different strains which he tested, thus showing an underlying hereditary basis for this susceptibility, and (2) that mice seem very much less susceptible than rats to this type of experimental neoplastic production, thus showing a racial hereditary tendency underlying this susceptibility.

In his report, No. V[17], he sets forth the difficulties he experienced in producing any experimental spiroptera cancer in mice, finally succeeding in securing only three such cases among hundreds of mice tested. He also states that he did not succeed in any case in producing spiroptera cancer in wild *mus musculus, mus sylvaticus,* or wild Norway rats *(mus decumanus).* He is forced to conclude from these negative results that there probably must be a predisposition to spiroptera cancer, determining the success or failure of this experiment both for different species and for different individuals.

Such an explanation of his results places them in perfect harmony with the fundamental influence of heredity in cancer susceptibility, observed and reported by this laboratory for the past twelve years. It is in complete conflict with the conclusions hastily reached by some scientists from Fibiger's early reports, that spiroptera carried a cancer germ, or was in some other way an essential agent in the causation of cancer.

Fibiger further states that spontaneous mammary gland carcinoma and mammary gland sarcoma have arisen in mice whose stomachs he had infested with spiroptera without securing stomach neoplasms.

This result is in harmony with the results in this laboratory of nematode-infested mice, which instead of tumors in the digestive tract develop tumors in the mammary gland, lung, liver, retroperitoneal tissues, etc., in accordance with their inherited potentiality and irrespective of nematode infestation.

That is, the presence of artificially introduced larvæ in the liver or stomach and intestines of rats and mice of spontaneous cancer strains, does not produce neoplasms in the liver or stomach or intestines necessarily, but spontaneous neoplasms arise in those organs which by inheritance lack the cancer-resistant mechanism, just as they do in this laboratory, whether or not mice have normally ingested nematodes.

It is extremely interesting and gratifying to find this striking harmony between the experimental spiroptera and liver sarcoma and spontaneous neoplasms in mice, whereby the demonstration of the inheritability of spontaneous cancer is corroborated by a line of work which seemed at first (to many) likely to show that experimental cancer could be produced at will in all animals, and which was taken by many commentators to indicate that the tendency to cancer might not, after all, be inheritable. These results lead us to hope that when the field of experimental cancer production has been more completely investigated, the most perfect harmony will be found to exist in every detail between such lines of work which experimentally produce true neoplasms, and the work with spontaneous cancer.

VII. PATHOLOGIC CHANGES FOLLOWING THE NORMAL INGESTION OF SPIROPTERA

There have been to date in this stock 61 cases of nematode infestation from normally ingested larvæ. Among these 61 mice there have been 10 with tumors and 1 with leukemia. There have, therefore, been 50 mice infested with nematodes, which have not shown neoplasms anywhere, nor have they shown leukemia or pseudoleukemia.

[16] Det. Kgl. Dan. Vid. Sel. Biol. Med., 1918, p. 22.
[17] Det. Kgl. Dan. Vid. Sel. Biol. Med., I, 1918, p. 11.

The tumors in mice with both nematodes and neoplasms, were distributed as follows:

Mammary gland	6	carcinomas
Lung	2	1 carcinoma 1 carcinoma and 1 adenoma
Liver	1	adenoma
Retroperitoneal	1	lymphosarcoma
Leukemia	1	
Total	11	tumors and leukemia

None of these mice infested with nematodes had tumors in the stomach or intestine, or in the mouth or tongue.

On the negative side, the evidence is still more striking. Of the 5,000 spontaneous tumors arising in this stock to date, only 10 were in mice infested with nematodes. There have been to date only 13 cases of neoplasms in the gastro-intestinal tract, among the mice in this laboratory. Of these, not one occurred in an animal infested with nematodes, tapeworm or any other discoverable parasite. Moreover, some of the mice with nematodes in the stomach were members of the strains carrying the few spontaneous stomach and intestinal tumors which have occurred in this stock.

There is a perfectly standard result of the normal ingestion of nematodes as shown by necropsies in this laboratory. These results are of a highly degenerative character and do not involve neoplastic proliferation in the gastro-intestinal tract or elsewhere, either in the tumor strains or in the non-tumor strains, not even in the tumor strains where the stomach and intestinal tumors have arisen.

It is interesting to note here, as in the case of tapeworm-infested mice, that the wild house mice and wild rats autopsied in this laboratory show exactly the same types of pathologic changes where they are infested with nematodes, as do the mice belonging to this stock.

Fibiger's results, in failing to obtain spiroptera cancer in wild *mus musculus*, *mus sylvaticus* and *mus decumanus*, even by the injection of 800 larvæ into the stomach at one time, is in beautiful harmony with these results obtained in this laboratory.

Two striking differences emerge in the results of artificial and of naturally ingested nematode larvæ: (1) Fibiger states that young rats and mice seem more susceptible than older animals. Bullock and Curtis make the same statement with reference to their experimental liver sarcoma. The reverse is true of spontaneous neoplasms both in rodents and in man. (2) Fibiger injected 300 to 800 larvæ into each of his animals. The highest number of nematodes ever found in an animal autopsied in this laboratory was eleven, in a wild house mouse. The average was four or five. Many of the animals had only one worm, and some of them two or three. Where the larger number of larvæ had been swallowed, they were not ingested at the same time, as the worms were in different stages of development.

Evidently this smaller number of worms does not furnish irritation of the type to overthrow the cancer-resistant mechanism, even in the stomach tumor strains, although even one worm is sufficient to cause fatal degenerative changes.

Assuming the nematodes to be the efficient cause of stomach cancer in all of Fibiger's cases, 300 to 800 worms would then be of the type to destroy the non-cancer mechanism in 54 rats and of three of the laboratory mice tested, but would not be of the type to destroy the cancer-resistant mechanism in most of the laboratory rats, all but three of the laboratory mice, and all of the wild rats and mice tested by Fibiger, just as the lower number of from one to eleven worms found in the laboratory mice in this stock, and all of the wild rats and mice of this vicinity autopsied, were not the type of irritation fitted to overthrow the cancer-resistant mechanism.

When this whole field of experimentally produced cancer has been thoroughly

worked over, *we shall probably find that predisposition to the type of tumor produced is the one fundamental essential, just as it is the one fundamental essential in spontaneous neoplasms.* Fibiger's meager results in securing spiroptera cancer in mice, even in mice of spontaneous cancer tendency, is in very strong corroboration of the hereditary nature of cancer.

We seem to have here, in this possibility of the overthrow of the cancer-resistant mechanism, a parallel with other cases of the overthrow of regenerative powers; for example, the power of the skin to regenerate a certain amount of burned area, but its overthrow in the presence of a larger burned area. Undoubtedly there is here also an underlying hereditary tendency to the capacity to regenerate a greater or a less amount of destroyed skin.

This difference in the reaction to naturally ingested worms numbering from one to eleven, and artificially ingested worms numbering from 300 to 800, seems further to corroborate the theory that the cancer tendency is due to the lack of a mechanism fitted to control proliferation and differentiation in regenerative processes. Apparently 300 to 800 worms is sometimes efficient in overthrowing this mechanism in some animals, probably in exact accordance with their inherited potentialities; although there is no evidence in Fibiger's reports that these same rats might not have developed gastric tumor from other causes than spiroptera; that is, they may have lacked the cancer-resistant mechanism in the stomach. That wild rats have been found showing stomach tumors where they had ingested nematodes and others where they had not ingested nematodes would indicate that rats are normally more susceptible to stomach tumors than are mice. This is another indication of the racial hereditary tendency underlying the development of neoplasms. From one to eleven worms have never to date been found efficient in overthrowing this mechanism, even in mice of gastric tumor strains; but if worms were the host of a specific cancer germ, one to eleven worms should be sufficient to introduce the germ.

The essential fundamental in which the artificial production of tumors differs from the spontaneous production of neoplasms, is that in the former case the experimenter destroys the normal metabolism of his animals by the violence of his methods of irritation, exactly as the pigment-making mechanism can be destroyed by a blow on the head. He is not, therefore, testing the behavior potentialities of his experimental animals under normal conditions. This violently destructive method of irritation, which overthrows such cancer-resistant mechanism as the attacked animal organ may possess, may very probably at the same time overthrow other metabolic mechanisms and relations upon which we might depend in a cancer therapy. That a much more wholesale destruction of cancer-resistant mechanism is effected in these experiments than obtains in spontaneous cancer, is shown by the vastly greater extent, for example, of Bullock and Curtis's experimental liver sarcoma than has occurred in any case of spontaneous liver tumors of any type, in this laboratory.

In my opinion Fibiger's results show that there is an inherited difference in the stability of this mechanism and the amount of violence necessary to overthrow it, in different races, different strains, and even in different individuals of the same strain; and his results justify the conclusion that there are some individuals, some strains, and even some whole races, in which the cancer-resistant mechanism cannot be overthrown by any violence short of fatal violence. Bullock and Curtis are evidently finding the same to be true of their experimental liver sarcoma.

VIII. TAR CANCERS

The first successful experimental production of tar cancer was reported by

Yamagiwa and Ichikawa[18] in 1915. Later Tsutsui[19] produced the same type of cancer in mice. Also Fibiger, and Fibiger and Bang[20] have obtained many such cancers in mice.

The infrequency of metastasis from these tar cancers is in harmony with the behavior of spontaneous squamous cell carcinomas of mice arising in this stock, which seldom produce metastasis, and also in harmony with the tar cancers produced by Yamagiwa in the ears of rabbits, which seldom showed metastasis.

IX. SPONTANEOUS SQUAMOUS CELL CARCINOMAS IN MICE

Among 40,370 autopsies performed in this laboratory, and given careful microscopic examination, 191 spontaneous squamous and basal cell carcinomas have occurred, none of them due to exposure to coal tar products of any sort. The location of these tumors was as follows:

Face, including muzzle skin, eyelids, mouth, ears, trunk.....	100
Mammary gland	65
Lower jaw	15
Stomach	5
Rectum	2
Vulva	2
Vagina	1
Lung	1
Total	191

Over 200 of these squamous cell carcinomas have occurred to date, but only those whose clinical diagnosis has been confirmed by microscopic study are included in this report.

Nearly all the tumors arising on the head and trunk were located at the site of a healed wound, often beneath the scar tissue. The tumors of the jaw and mouth apparently resulted in many instances from the irritation of broken or irregular teeth. The carcinomas of the muzzle skin were almost uniformly founded upon a chronic and constantly scratched dermatitis.

The number of metastasizing tumors obtained by painting with coal tar is greater than from these spontaneous squamous tumors; another indication of the greater violence of the experimental method, and the more widespread overthrow of the cancer-resistant mechanism.

Fibiger's notable failure to produce more than three spiroptera cancers in the stomachs of mice has caused him to throw most of his efforts recently toward producing tar cancers of the skin in mice. His report, issued in 1921, on this work, is favorable to such experimental cancer production. When he has followed this line of experiment with the same care, the same length of time, and the same diversity of animal subjects of the experimentation which he used in his spiroptera experiments, he will doubtless find that here, also, the essential fundamental factor necessary to cancer production of this sort is the hereditary predisposition of the animal, and of the race to the kind of cancer attempted. The beautiful harmony between his results in spiroptera cancer and the spontaneous stomach and intestinal cancers in this stock, will then probably be duplicated by a similar harmony between his results in experimental tar cancer and the spontaneous squamous cell carcinomas of the skin, *arising from various types of chronic irritations,* in this stock.

The mouse is rather susceptible to squamous cell carcinomas of the skin. It is probable that in any set of laboratory mice procurable on the market, a large number will be by heredity predisposed to squamous cell cancers of the skin. More success in producing skin cancers experimentally in mice, either by coal tar products or by many other possible methods, may therefore confidently be looked for, than stomach and intestinal cancers, which are rare in mice.

[18] Mittheil. der Med. Fak. Univ. Tokyo, Bd. XV, 1915; Bd. XVII, 1917; Bd. XIX, 1918; Jour. Can. Res., III, 1918.

[19] Zeit. fur Krebs., XII, 1918, p. 2.

[20] Det. Kgl. Dan. Vid. Sel. Biol. Med., III, 1921, p. 4.

The longer these experiments in the experimental production of cancer are carried on, and the more thoroughly they are tested out, the more certainly and completely (in the opinion of the author) will they be found to harmonize with the fundamental facts of spontaneous cancer, when the tumors produced are true neoplasms. *Since heredity is a certain and fundamental underlying factor in the occurrence of spontaneous cancer, it must inevitably in every case of true experimental cancer of the tissues of the animal itself, also be found to be a certain fundamental factor.*

A synthetic consideration, then, of the results so far obtained in the experimental production of cancer, and in the spontaneous production of cancer, shows a striking harmony between these two in all fundamentals.

Along with these encouraging harmonies in fundamentals, there are also fundamental differences, and the probable overthrow of other normal and probably vital mechanisms by the same experimental violence which overthrows the cancer-resistant mechanism, must be taken into consideration in all conclusions regarding the etiology of cancer, and all cancer therapy.

It has been stated that probably no two spontaneous tumors are identical in structure, and that grafted tumors can teach us many things better than spontaneous tumors can, because the implants are structurally identical with the original tumor. This argument of the microscopist might possibly be put forth regarding all other experimental tumors of a given type, that is, they would probably be very similar to one another. There is no doubt, however, that all spontaneous neoplasms of a given type and of a given organ are identical in fundamentals, and differ only in minutiæ. This possible divergence in minutiæ should not interfere with our learning from them, just as we can learn the fundamentals concerning the structure and biologic behavior of any organic entity, although no two of any given organism, or any given organ, are identical. It seems far more essential that the metabolic conditions surrounding the origin and progress of the tumor should be the fundamental inherent conditions of the animal's tissues, as they are in spontaneous neoplasms, and not altered as they must be by experimentally produced tumors, rather than that the minutiæ of tumor types should be identical. The alteration of the metabolic conditions surrounding the experimental tumor seems to the author to be a serious handicap, both in the study of the etiology of tumors and of cancer therapy.

It remains to be seen whether or not it is possible so to strengthen the hereditary cancer resistance—that is, to strengthen the normal regenerative power—that it will be impossible to overthrow it. That is, is it possible, by the right selective breeding, to evolve a strain whose normal regenerative powers cannot be overthrown by the most violent or long-continued irritation, even of the experimental type (short of fatal violence)? It remains also to be seen whether or not it is possible to insinuate into the metabolism an increased stability of normal regenerative power, and consequent cancer resistance. In the light of our present knowledge of cancer, this would seem to be the most hopeful preventive method in the treatment of individuals of known inherited cancer tendency.

SUMMARY

1. Certain fundamental harmonies and certain fundamental differences exist between spontaneous neoplasms and all artificially produced tumors.

2. The essential harmony in all these is the fact that all tumors, both spontaneous and experimental, have been shown to depend fundamentally upon the inherited predisposition of the animal's tissues.

(A) In grafted tumors, *the success of the experiment depends fundamentally upon the inherited tendency of the animal's tissues to regenerate normally* and furnish proper conditions of attachment and food,

instead of abnormally, as is the case in spontaneous cancer.

(B) In liver, stomach and intestinal tumors resulting from parasitic infestation, *the success of the experiment depends upon the inherited tendency of the animal's tissues to attempt regeneration under such irritation*, and the violence of the method which overthrows such normal regenerative powers as the animal's tissues may possess. Many animals and many strains thus far tested, both by artificially introduced and by naturally ingested parasites, have been unable to regenerate the irritated tissues either normally or abnormally, and their organs have merely gone to pieces in degenerative changes.

(C) From tar painting, the same type of squamous cell carcinomas of the skin arises, as arises spontaneously from similar chronic skin lesions in mice produced by many other causes, and in all probability when this type of experiment has been thoroughly tested out, it will be found to depend upon the inherited tendency to skin carcinoma, which could equally well be produced by other types of chronic attacks upon a susceptible skin.

3. The fundamental difference between spontaneous neoplasms and all artificially produced tumors, seems to be that the spontaneous tumor is the product of the animal's own inherent metabolism, that is, the inherited tendency to regenerate abnormally under various assaults upon the tissues; while, to date, all experimentally produced tumors seem to indicate that the violence of the method may have overthrown inherent cancer-resistant mechanisms, with the probability at the same time of the overthrow of other vital fundamental metabolic mechanisms.

4. These harmonies between spontaneous and artificially produced tumors give promise that it may be possible to strengthen the cancer-resistant mechanism, since there seem to be varied grades of such resistant mechanisms, and there are evidently resistant mechanisms that cannot be overthrown by the most violent and long-continued methods yet attempted.

Radiation therapy and surgery.—No field of surgery is more discouraging than operation for cancer of the cervix; statistics the world over demonstrate this. In the Gynecologic Department of the University Hospital, there has never been more than 33 per cent of five-years in a relatively small number of operative cases culled from a much larger group of surgically hopeless cases.

In the outset radium was used very cautiously, first in the hopelessly inoperable cases, and then in the borderline cases. The results in these were so encouraging that surgery is now used only in the absolutely favorable cases, which have been so few as to be almost negligible.

Statistical reports are misleading because of the wide variation in what are regarded as operable cases; Peterson finds 15.7 per cent operable, while Graves finds 65 per cent operable; also the operation varies, because the primary mortality varies from 5 per cent to 26.6 per cent. The only way of estimating cures is on the basis of gross numbers.

The statistics of ten surgeons reporting on surgical results are compared with those of five surgeons reporting on radiation therapy, together with the results in the hands of the authors in 144 cases, with the conclusion that radiation challenges most favorable comparison with the radical abdominal operation, but skillful surgery followed by post-operative irradiation cannot yet be criticized. To discard or fail to use radiation as an adjunct to surgical measures in the face of the available statistics should lay the operator open to a charge of criminal negligence.

W. W. WATKINS, M.D.

Relative Values of Irradiation and Radical Hysterectomy for Cancer of the Cervix. John G. Clark and Frank B. Block. Atlantic Med. Jour., Aug., 1924, p. 696.

QUANTITATIVE FACTORS IN THE SUSCEPTIBILITY OF LIVING CELLS TO EXTERNAL AGENTS[1]

By C. M. CHILD, PH.D.

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THE pharmacologist and the mammalian physiologist have found that the susceptibilities of particular organs and parts of the mammalian body to many external agents are apparently highly specific. Very commonly a distinction is made between agents showing apparently specific action on particular parts and those acting on living protoplasm in general, but at the same time the fact is generally recognized that any agent in sufficient concentration or degree of action and with sufficient time may act as a general protoplasmic agent and affect all organs or parts, even though its less extreme effects are apparently highly specific. But in so complex an organism as man or any other mammal it is usually impossible to determine with accuracy the concentration or degree of action of a particular agent to which a particular organ may be exposed at a given time. This is true whether the agent is introduced through the alimentary tract, the blood stream, the lymph or the body surface. Consequently the possibility exists that some of the apparently specific effects of certain agents may be due in some measure to the fact that different parts are exposed to very different concentrations or degrees of action.

As regards the effects of various agents on development and growth, it is a well known fact that absence of a particular element or compound which is essential for development of a particular part may determine a specific modification, that is, absence of the part and perhaps of other parts whose development is dependent on its presence. For example, various marine animals which develop skeletal structures of calcium carbonate remain without skeletons in calcium-free sea water, and certain parts whose development is dependent on the growth of the skeleton fail to appear. Also the more or less specific effects on later development and growth of diets deficient in one or more of the vitamins, or other essential substances, have been repeatedly demonstrated. Various endocrine substances are known to influence growth and larval metamorphosis, even in other species than those from which they are derived, but many facts seem to indicate that these effects are not, strictly speaking, specific: they appear to result rather from alterations in the rate of general metabolism than from specific action in the strict sense. The work of Guyer and Smith on the production of more or less hereditary eye defects in the offspring of rabbits injected with lens antibodies seems to indicate that the mammalian germ cell or embryo may be specifically affected by parental antibodies, though even in this case the possibility exists that the effect is not specific in the strict sense.

Without questioning the existence or significance of specific susceptibilities of particular organs to particular agents in the higher animals and man, the present purpose is to call attention to another more general aspect of the problem of protoplasmic susceptibility to external agents. Extensive experimental investigation has shown that the susceptibility of many of the simpler organisms, both animal and plant, and the earlier developmental stages of even the higher animals to more or less toxic or injurious concentrations or degrees of action of many, perhaps of all, external agents which are capable of acting on protoplasm, shows certain features which are to a high degree non-specific for different agents. In other words, certain individuals of a species or certain regions of

[1] Read at the mid-annual meeting of the Radiological Society of North America, Chicago, June 6, 1924.

the individual body are in general more susceptible, others less susceptible, to many different agents, though the amount of difference may differ for different agents.

Such non-specific differences in susceptibility are associated with differences in physiological age and with differences in growth, excitatory and other functional activity. Moreover, we find that the axes of physiological polarity and symmetry of the whole body and of axiate organs and parts are primarily represented by characteristic non-specific differences in susceptibility which are definitely related to the course of development and differentiation.

Such differences in susceptibility must depend on differences of some sort in the physiological condition of the protoplasms concerned. Their non-specific character as regards different agents and their relation to differences in degree of excitation, functional activity and growth, suggest the probability that they depend primarily on quantitative rather than on qualitative factors in physiological condition, and experimental investigation shows that this is the case.

METHODS OF DETERMINING SUSCEPTIBILITY

Before taking up the results of investigation along these lines it is necessary to mention briefly the chief methods by which susceptibility can be determined. With concentrations or degrees of action which are above the limit of tolerance but which do not kill instantaneously susceptibility can be directly determined in many organisms by survival time. The shorter the survival time the greater the susceptibility and *vice versa*. As regards determination of the time of death, it is important to note that in the simpler forms and the earlier developmental stages death of the organism does not occur except as death of its cells and tissues takes place. The apical or anterior region may die while basal or posterior regions are still alive and functionally active. In such cases there is no definite time of death of the organism as a whole, determined by the cessation of function of some essential organ, as in the higher animals and man, but only the death of the tissues or cells, or, in unicellular forms, of different regions of the cell. The approximate time of such death may be determined in various ways. For example, death of naked cells in many agents is closely associated with cytolysis or protoplasmic disintegration, which is clearly visible. In some other cases visible coagulations occur with loss of the characteristic structure. Again, cytolysis of the dead parts may occur on removal to water or some other agent after treatment with a certain agent. In still other cases vital dyes which are not held after death of the protoplasm can be used. On the other hand, dyes which do not penetrate living protoplasm but which rapidly stain dead protoplasm are of value in many cases.

In determining susceptibility to chemical agents it is necessary to provide as far as possible for equal exposure to the agent of different regions of the body to be tested. In naked aquatic forms with little differentiation of different regions of the body surface, susceptibility of the surface to chemical agents can be directly determined by placing the organism in a solution of proper concentration of the agent in the normal medium and providing for sufficient agitation to keep the concentration uniform on all parts. In many eggs of marine forms, in unicellular organisms, and in naked free-swimming developmental stages, blastulæ, gastrulæ and larvæ of many aquatic forms, the differences in susceptibility of different regions of the surface can be directly observed and compared in this way. In more highly differentiated organisms with more or less complex internal organs the susceptibilities of these organs to chemical agents cannot be directly determined by such methods, because the agent must reach them either by passing in through the body surface generally or by entering through respiratory or alimentary surfaces. Under such conditions equal exposure of the internal or-

gans cannot be provided for. In many of the lower invertebrates these difficulties may be overcome in part by exposure to the agent of cut surfaces from different body levels. Also when the body is covered by a cuticle or an exoskeleton, cut surfaces may assist in determining differences.

In early developmental stages the effect of the agent on rate of development can also be used as an indicator of susceptibility. For example, with inhibiting agents the regions which are most susceptible to lethal concentrations or degrees of action are most inhibited in development in somewhat lower concentrations, and *vice versa*. Extensive modification of development with production of monsters of certain definite kinds results from such differential inhibition of development.

These different ways of determining susceptibility are all modifications of what has been called the direct method, because the differences in susceptibility are directly determined by the lethal or toxic action of the agent. The range of concentration or degree of action available for this method lies between that immediately lethal for all parts or individuals concerned and that which permits certain regions or individuals to acquire tolerance or become acclimated.

Living protoplasm possesses the ability to acquire tolerance or, in general biological terms, to acclimate to a certain range of relatively low concentration or degree of action of many external agents and to recover after temporary exposure within certain limits of concentration or degrees of action and time. These capacities for acclimation or acquirement of tolerance and for recovery provide a basis for an indirect method of investigating susceptibility. For example, certain regions or individuals acclimate or acquire tolerance more rapidly or to a greater degree to a certain nonlethal range, or recover more rapidly or more completely after temporary exposure. In fact, with a certain range of concentration or degree of action one region of the body may acclimate or recover and continue to live, while another may fail to do so and may finally die. In mature forms acclimation and recovery may be indicated by increased motor or respiratory activity after an initial decrease, and by various other physiological changes showing reversal of a primary effect. In the earlier developmental stages acclimation and recovery may be indicated by increase in rate of growth and differentiation after an initial decrease, and in such cases modifications of development in the opposite direction from those produced by the primary action of the agent may be brought about.

These general susceptibility relations have been studied in several hundred species of animals and plants, including among the animals at least the earlier developmental stages of members of all the great groups. The agents used in this investigation include the following: potassium and sodium cyanide; many anesthetics, such as ethyl alcohol, ethyl ether, ethyl urethane, chloretone, chloral hydrate, chloroform; strong and weak acids; strong and weak bases; carbon dioxide; many inorganic salts, including salts of sodium, potassium, lithium, magnesium, copper, mercury, etc.; the alkaloids caffein, strychnin, atropin; various somewhat toxic vital dyes, such as methylene blue, neutral red, Janus green; the negative condition, lack of oxygen; extremes of temperature; ultra-violet radiation, and visible light after photochemical sensitization by means of various substances, such as eosin; and, finally, a few preliminary experiments with radium radiation, particularly the beta rays. By no means every one of these agents has been used on every species and every stage examined, but enough comparative work has been done to make it certain that to a certain range of concentration or degree of action of all of these agents differences in susceptibility of different body regions of the individual and of individuals of the species in different physiological condition exist, which are not specific for different agents, though they may differ in amount.

PHYSIOLOGICAL BASIS OF NON-SPECIFIC DIFFERENCES IN SUSCEPTIBILITY

In general, we find that rapidly growing and functionally active regions or individuals are more susceptible than less active to a certain range of lethal or highly toxic concentrations or degrees of action, and that these same regions or individuals acclimate to, or recover from, the action of a lower range of concentration or degree of action more rapidly or more completely than do the less active. These facts alone suggest that quantitative differences in metabolic activity and associated conditions may be factors in determining such differences in susceptibility. Comparison between susceptibility to the cyanides and their action in inhibiting physiological oxidations and between susceptibility to cyanide and to lack of oxygen also suggests a relation between susceptibility and a quantitative metabolic factor.

Various other experimental methods confirm these suggestions and make it possible to check the results of the susceptibility method. For example, it has been possible to show in various cases by direct determination of oxygen consumption and by colorimetric estimation of carbon dioxide production that susceptibility does vary with respiratory rate. Various oxidation-reduction reactions, *e.g.*, the reduction of potassium permanganate by protoplasm, the formation of indophenol, an oxidation catalyzed by oxidizing enzymes, and the reduction of vital dyes (such as methylene blue) also afford evidence for the existence of a relation between susceptibility and rate of oxidative metabolism. Regional and individual differences in rate of such reactions, or in total amount of product as indicated by color, correspond to non-specific differences in susceptibility. Differences in electric potential in different regions of the body also show a definite relation to differences in susceptibility. And, finally, it has been shown that these non-specific differences in susceptibility cannot depend solely or primarily on differences in permeability of limiting surfaces to the agents used, for the differences in susceptibility are similar for substances which penetrate living membranes readily without producing appreciable injury, for substances which do not penetrate living normal membranes in appreciable quantities, but which destroy irreversibly the physiological permeability as they enter, and finally, for agents such as extremes of temperature, the negative condition, lack of oxygen, visible light after sensitization, ultra-violet and radium radiation, in the action of which permeability is not directly concerned.

The general conclusions concerning the relation between susceptibility and physiological condition to which the facts at hand point are as follows: Differences in susceptibility of body regions or individuals which are non-specific for different agents must depend on quantitative rather than on specific differences in physiological condition, and investigation has shown that, in general, a relation between such susceptibility and rate of cellular respiration, or of oxidative metabolism, exists. In other words, the rate of cellular respiration, or oxidative metabolism, serves in some measure as an index of the physiological differences on which the non-specific differences in susceptibility depend. But the relation between susceptibility and quantitative metabolic factors appears in two different aspects: First, to a certain range of concentration or degree of action which is above the limit of tolerance or acclimation and is gradually lethal or produces irreversible effects with continuous exposure, or effects only slowly reversible after temporary exposure, susceptibility varies in general directly with, though not necessarily proportionally to, rate of respiration, or oxidative metabolism; second, to a certain range of lower concentrations or degrees of action the ability to acclimate or acquire tolerance varies directly with, though not necessarily proportionally to, rate of respiration, or of oxidative metabolism; third, the ability to recover after temporary ex-

posure to a certain range of concentration or degree of action also varies directly with, though not necessarily proportionally to, rate of respiration or oxidation. In other words, non-specific susceptibility appears to be associated in some way with quantitative metabolic factors.

The question at once arises as to the nature and basis of this relation. The fact that regions of high oxidative metabolism are more susceptible than those of low to certain concentrations of many agents and more capable of acclimating to or recovering from the action of certain other concentrations certainly cannot mean that the action of all the different agents on protoplasm is the same in kind and differs only in degree. Although much remains to be learned concerning the action of external agents on protoplasm, it is certain that different agents act in very different ways. Certain agents may affect protoplasms through their ionizing action, others certainly have no such action; some may swell, others may decrease, the volume of the protoplasms; some may act on certain or on all enzymes, and some may enter into certain chemical reactions, while others may affect the velocity or the character of reactions in other ways. Evidently the non-specific differences in susceptibility must be largely or wholly independent of such differences in action.

At present the relation between susceptibility and quantitative physiological factors appears to be a case of a sort of relation between systems undergoing dynamic equilibration and disturbances of such systems which is found in more or less analogous form in many non-living systems. In the case of a flowing stream, for example, a disturbance sufficient to divert or stop the flow of the stream, *e.g.*, a diversion channel, a dam, a landslide, will produce its effects, diversion, formation of a lake, draining of the channel below the dam or obstruction, more rapidly in a rapidly flowing than in a slowly flowing stream. Conversely, the rapidly flowing stream will equilibrate more rapidly than the slowly flowing to slight or temporary disturbances which do not destroy or irreversibly alter the stream, but bring about slight or temporary changes. If we introduce a partial barrier of rocks which the stream cannot remove, the adjustment of levels, currents, etc., to the altered situation will occur more rapidly in the rapid than in the slow stream, and if the partial barrier be of sand the rapid stream will remove it more quickly than the slow stream.

Again, if we conceive a series of changes or processes, each of which depends in some measure on the preceding member of the series, *e.g.*, the various steps in the fabrication of an industrial product or a series of chemical reactions, it is evident that within certain limits the relations between velocity and effect of disturbance on the system will be similar to those in the case of the flowing stream. The higher the speed of the processes or reactions, the more rapidly will extreme disturbance of any one of them disrupt or transform such systems, and the more rapidly will equilibration to slight degrees of disturbance, or recovery from temporary reversible disturbances, occur.

Living protoplasms are extremely complex systems in process of dynamic equilibration to external factors. The chemical reactions and other processes and conditions in protoplasms are not independent of each other and disturbance of any one of the essential factors, whether a chemical reaction or a physical condition, must sooner or later affect the whole system, and it is evident that when the effect of the disturbance is extreme and irreversible, the effect on the protoplasm as a whole must occur more rapidly when the changes characteristic of life are proceeding rapidly than when they are proceeding slowly. Acclimation to and recovery from external disturbances are brought about in protoplasm in various ways. Acids and bases are neutralized, some toxic substances are oxidized, some are reduced, some are de-

composed or altered in other ways, but whatever the process concerned it is associated in some way with the changes characteristic of life, and the protoplasm in which these changes are proceeding rapidly must in general acclimate or recover more rapidly than that in which they are proceeding slowly.

This appears to be the basis of the general non-specific susceptibility relations. Different agents may act primarily on different reactions or other factors of the protoplasmic system, but however they act, it appears that within certain limits the susceptibility of the protoplasm must vary, as stated above, with the fundamental dynamic factors characteristic of it.

In protoplasmic systems which are qualitatively or specifically different, the differences in susceptibility may also be more or less specific. In different organs of the higher animals and man, qualitative or specific differences in constitution and metabolism may be very great, *e.g.*, in brain, liver and thyroid, and the susceptibilities of such different organs may be highly specific for different agents, but within a particular organ, or, more strictly speaking, a particular kind of tissue, the non-specific susceptibility relations appear. As we pass from the more complex to the simpler animals and from later to earlier stages of development, the qualitative or specific differences of different parts become progressively less, consequently the specific susceptibilities of the higher forms and later stages are replaced more and more generally by the non-specific relations. In fact, the evidence from the susceptibility method, and the other methods of investigation available, leads us to the conclusion that the physiological axes of polarity and symmetry in organisms are primarily quantitative gradients in physiological condition and activity. In other words, the axiate individual in its simplest terms consists in such a physiological gradient in one or more directions in a protoplasm of specific constitution, and the qualitative or specific differences of different organs and parts arise secondarily in consequence of the different conditions at different levels of such gradients.[2]

EXPERIMENTAL INVESTIGATION AND ANALYSIS OF SUSCEPTIBILITY

It is evident from what has been said that in order to make intelligent use of the action of any external agent on protoplasm we need to know not only the nature of the physico-chemical changes directly produced by the agent, but the relation of such changes to the protoplasmic system on which the agent acts. Investigation of the relations between susceptibility to the action of external agents and the quantitative and qualitative factors of physiological condition constitutes one method of attack on this problem, but such investigation involves far more than the mere determination of the existence of differences in susceptibility or of a certain degree of susceptibility. Some of the things we need to know in the physiological analysis of protoplasmic susceptibility may be briefly pointed out. Suppose, for example, that we observe differences in the susceptibility of different organs or body regions to the action of some agent in a certain concentration, intensity or dosage. Such an observation does not tell us whether the observed differences are dependent upon differences in the direct action of the agent or upon differences in the ability of the parts to acclimate or acquire tolerance or to recover, nor does it tell us whether the observed differences are dependent upon quantitative or upon specific differences in the protoplasms concerned.

We must, first of all, determine susceptibility differences for a wide range of concentrations or degrees of action, from those which kill immediately to those which have no toxic effect. When the differences in susceptibility depend primarily or chiefly upon quantitative protoplasmic differences

[2] For a more extended discussion of the non-specific aspects of susceptibility, with bibliography, see Child, *Physiological Foundations of Behavior*, New York, 1924, Chapters VII-IX, and references there cited.

we find that for certain different ranges of concentration or degree of action of most agents the differences in susceptibility are opposite. In the higher range the difference represents the difference in direct toxic or lethal effect; in the lower range it represents the difference in ability of the protoplasms to acclimate or recover. There may be some agents whose action permits no appreciable degree of acclimation or recovery, but this is by no means certain. On the other hand, it is evident that protoplasms do possess a remarkable capacity to acclimate to and recover from the action of a very large number of external agents.

Second, the differences in susceptibility to one agent must be compared with the differences to others in the various effective concentrations or degrees of action. If we find that the differences in susceptibility to directly lethal or strongly toxic action, on the one hand, and the differences in ability to acclimate or recover, on the other, are similar for different agents which act in different ways, we have some evidence for the conclusion that the differences in susceptibility are primarily due to non-specific quantitative physiological differences, and the value of this evidence increases with the number of agents used and the variety of checks possible by other methods.

Such checks by other methods are highly desirable. We must investigate the quantitative and specific differences of the regions or parts concerned, *e.g.*, by determining quantitative and qualitative differences in metabolism and in physico-chemical constitution and their relations to the differences in susceptibility, and by determining the effect on susceptibility of experimental alterations of rate of metabolism.

Moreover, it does not follow that because differences in susceptibility to a particular agent are found to be non-specific in a particular case and for a particular agent that they will be so in other cases. As already noted, differences in susceptibility may be highly specific in certain organs of the higher animals in maturity or later developmental stages, and highly non-specific for many different agents in less highly specialized tissues, earlier stages of development, or simpler forms. Again, susceptibility of certain parts may be specific for certain concentrations or degrees of action and non-specific for others. For example, a region containing much fat or lipoid may be specifically highly susceptible to certain concentrations of fat-soluble substance, because such substances attain a higher concentration in that region than elsewhere, but to certain other concentrations of the same agent the fat-containing region may be less susceptible than a more active region. Many agents accelerate or stimulate, at least at first, in low, and inhibit in high concentrations or degrees of action. This is true even of many, if not of all, the so-called stimulating agents, *e.g.*, alkaloids, such as strychnin, caffein, etc., and it is also true in some degree for such general protoplasmic poisons as the cyanides.

These are some of the physiological aspects of the problem of susceptibility as it appears at present. The radiologist is interested in certain aspects of this problem, more particularly in the differences in susceptibility to radiation of pathological and normal cells, and most of all, perhaps, in those between the cells of malignant neoplasms and normal cells. While the data now at hand concerning radiation do not permit us to draw final conclusions, there is no reason to believe that the physiological basis of differences in susceptibility to any form of radio-activity is fundamentally different from that of susceptibility to other agents. The data are still fragmentary, but at present they indicate that non-specific quantitative physiological differences are important factors in determining differences in susceptibility to radiation. As in the case of other agents, regions or individuals with a higher rate of oxidative metabolism are in general more susceptible to the lethal or toxic action, and at least in some cases more capable of acquiring tolerance to, or of recovery from less extreme

degrees of action, though the reversibility of the effects appears to be slight for some forms of radiation. At present there seems to be no conclusive evidence that the differential susceptibility of tumor cells and normal tissue cells is anything more than this. The tumor cell, particularly the cancer cell, is apparently a much more active cell than the normal tissue cell, and, therefore, more susceptible to more extreme effects of external agents. If we could provide for equal exposure to other agents in the same degree as to radiation, we should probably find that the differences in susceptibility between cancer cells and normal cells would be similar for certain ranges of other agents and for radiation, though they might differ in amount.

The difference in susceptibility corresponding to a given physiological difference is greater for some agents than for others, and the facts at hand indicate that it is very great for at least certain ranges of the action of some forms of radiation. For example, preliminary experiments have shown that the physiological differences at different levels of the polar axis of certain of the lower invertebrates correspond to differences of several weeks in survival time with certain exposures to the beta rays of radium, while with a one-thousandth molecular solution of potassium cyanide the physiological differences are represented by differences in survival time of a few hours and with a two-hundredth molecular hydrochloric acid, by differences of a few minutes. Probably the value of radiation in medicine is in some measure due to this high differential, in consequence of which a dosage sufficient to kill or inhibit the active cells of a neoplasm does very little or no lasting damage to the normal tissues.

There are also various facts which indicate that radiation, like at least many other agents, in sufficiently low dosage accelerates cellular activities, or certain of them. And finally, the fact that differences in susceptibility to radiation are non-specific in certain cases, under certain conditions does not exclude the possibility that in other cases or under other conditions they may be specific.

This brief survey is merely an attempt to call attention to some of the more important aspects of the problem of protoplasmic susceptibility as it appears to us at present. The chief emphasis has been laid upon the non-specific or quantitative factors because these apparently represent the general physiological basis of susceptibility, while the specific differences, within a particular species-protoplasm, so far as they exist, are apparently secondary.

DISCUSSION

DR. B. C. DARLING (New York): If I caught the drift of these papers, it is more that of the origin and cause of cancer than the use of the X-ray to cure it. At least I want to get over to that side of the thing. I want to ask all and sundry and the world whether they have found anything definite to show that trauma produces malignant disease—sarcoma or cancer. There is a general drift in that direction, especially noted in certain quarters, and until somebody can show me that the patella has more cancers than the shin bone and the anterior bone has more cancers than those protected parts which sarcomas seem to select, I will continue to feel that trauma is not the cause of malignant disease.

I want to call attention to the use of the word "trauma," as synonymous with the word "irritation," especially by Dr. Sittenfield. I have a complaint to make about taking specific terms and using them as parallels with a generalized term. For instance, Dr. Sittenfield talks about "irritation" and "trauma" more or less as synonyms, and then he talks about a "traumatized cell" or a "traumatized area." "Irritation," to my mind, means "stimulation." It is more or less of a chemical or heat stimulation. I am hunting trouble, I suppose, in talking in this way, but maybe he can teach me something. Trauma is a spe-

cific insult to tissue in the way of abrasion, contusion, incision or laceration, unless I am off again. Now an irritation is not a contusion nor an abrasion, and I think we ought to purge our literature of any such transposition of terms.

I am interested now in finding out whether trauma causes newgrowth, and I do not believe it does. I do believe there is a great deal of chronic irritation which produces a hyperplasia, a stimulation and overaction, and consequently could produce, to my mind, newgrowth, but trauma is an entirely different proposition.

PROF. C. M. CHILD (closing): A brief further statement may serve to bring out more clearly the distinction between the quantitative and the qualitative aspects of the susceptibility problem. In cells or tissues which are specifically or qualitatively different from each other we may expect to find specific or qualitative differences in susceptibility to different agents. But when we are dealing with one particular kind of tissue, consisting of a particular kind of protoplasm, whether it be the tissue of a simple organism, an early embryonic stage, or a tissue of some particular organ of a mammal or man, we find much evidence that susceptibility depends primarily upon the degree of physiological activity of the tissue. In such a case differences in susceptibility in different regions or in different masses of the tissue depend primarily on quantitative physiological differences and are not specific for particular agents, but, at least within a certain range of concentration or degree of action of the agent, are similar for many, if not for all agents.

There is at present no evidence to indicate that the high susceptibility of the cancer cell to radiation as compared with the cells of normal tissues depends either on its own specific constitution or on the specific action of radiation. As an extremely active cell we may expect it to be highly susceptible as compared with ordinary body cells to sufficiently high dosage of external agents generally. If in any way we decrease its activity we decrease its susceptibility. It has been observed that cancer cells in tissue culture are less susceptible than those *in situ*. While we have as yet no certain evidence on the point, it is highly probable that under the conditions of tissue culture the metabolism of the cells is very considerably decreased and that the decreased susceptibility results from the decreased activity.

DR. H. H. BOWING (Rochester, Minnesota): For your information, I would like to say that Dr. Broders is responsible for the valuable data concerning the grading of tumors. The surgeons of the Mayo Clinic have appreciated the importance of this work, and the surgical procedures undertaken in a given case depend largely on the pathologist's report on the tissue sectioned at the time of operation. The grade of malignancy is very important when a diagnosis of malignancy is made, so we as specialists in the treatment of neoplastic disease must appreciate its importance and be guided accordingly.

Grade 4 tumors are rapidly growing, highly malignant tumors, whereas Grade 1 tumors are slow-growing and only slightly malignant. Grades 2 and 3 fall between these two extremes. A wide removal of the disease in Grade 1 will cure the patient, but in Group 4, palliation is all that can be expected from a similar procedure.

The radiologist treating neoplastic disease must also learn, as the surgeon has, to appreciate the grade of malignancy of tumors before outlining treatment.

The conditions on which the grading is based can be produced in tumor tissue through the action of radium and roentgen rays. Apparently we have agents at our command which will hasten or enhance the natural defense mechanism of the body. The idea that a lethal dose or carcinoma dose is essential to effect a cure must be changed. Since the body uses these agents to control the neoplastic disease, we as radiotherapists should understand, as much

as possible, the process in order that it may be accelerated and not destroyed. Individual treatment seems to be paramount, since these factors vary in each individual case.

I have endeavored to confirm the work of Alters, showing that differentiation in the malignant cell can be hastened, and the supporting matrix or stroma made to react to the invading malignant cell. The latter is characterized by the leukocytic infiltration fibrosis and eventually by hyalin formation.

The reduction in the primary tumor is usually associated with marked general improvement of the patient, thus reducing the surgical risk, should an operation be necessary. The time necessary for this favorable response to treatment varies with different persons, but is usually several weeks.

I am in hearty accord with the remarks of Dr. Sittenfield regarding the papers of Dr. Child and Dr. Slye, and am very grateful for the opportunity of listening to them.

Dr. J. D. Morgan (Philadelphia): In answer to the question of Dr. Darling—only a few days ago I saw a case of a man who had received a cut on his lip from a razor, some two years ago, as he was being shaved. It was treated in the usual way and apparently healed up. Gradually, however, the area became indurated, and swelled until it reached the size of a small olive. For the last year there had been no apparent change. When I saw it, the other day, there was a crust on the outside, and it was impossible to say whether it was malignant or some sort of a cyst, sebaceous or otherwise. At any rate, careful microscopic examination of a section showed it to be a small round-cell sarcoma. We have evidence here of trauma apparently producing a sarcoma, and in a very unusual place.

Dr. Darling: Was he a pipe smoker?

Dr. Morgan: No, he did not smoke to excess; there was no indication that this was at all the cause of irritation.

Dr. Henry Schmitz (Chicago): It is very unfortunate that the nomenclature of carcinomata is not uniform and pathologists and clinicians have a difficult time to grasp the meaning of discourses, as those given to-day. A way out of this difficulty would be to call all epithelial cell cancers carcinomata; then state (1) whether the cells are unripe, middle-ripe or ripe; (2) the elementary character of the cell, whether squamous, cylindrical, and so forth, and (3) whether medullary, simple or scirrhous and solid glandular or adenomatous, and so on. The proliferating, infiltrating or ulcerating character of the tumor is usually associated with a distinct cell group and structure. The clinical picture and prognosis, also, vary ordinarily with the structural and cellular characteristics. Therefore it is not surprising that the behavior of carcinomata to radiations differs.

Investigations made in our clinic will revolutionize radiation therapy, provided that carcinomata are excesses of growth of autonomous character of unknown etiology and origin. Though we do not as yet know the actual direct cause of tumors, in spite of the vast amount of research carried out, it is evident that Virchow's theory of persistent chronic irritations is more and more recognized as one of the chief causes of cancer. The tar cancers and Fibiger's experiments have confirmed the theory. The chronic irritation apparently causes a point of lessened resistance.

This, however, does not as yet explain the direct cause of the growth. We know that carcinoma carriers have lost the carcinolytic powers present in the serum of healthy individuals. This was proven by Freund and Kaminer and corroborated by Koritschoner and Morgenstern and Arnold and Schmitz. Nuzum and Glover, amongst others, have obtained from carcinoma tumors an organism which they claim to be specific. Both have produced typical carcinomata with glandular metastases in many animals. They have also obtained an antitoxin from their cultures and by its use

observed recessions of the growth. If these experiments should prove to be true, then carcinoma must be considered an infectious disease. These investigations are of a far-reaching value. Cause and treatment would then be successfully solved. Of course the improvement seen in cancers with serum treatment might be a protoplasma activation, as observed in non-specific protein therapy.

Clinical observations support the theories of chronic irritation and infectious nature. Women who are sterile or have few children have cancer of the cervix oftener than women with many children. In our series of 400 consecutive cervical carcinomata, women with three or fewer children numbered 66 per cent. We know that sterility results chiefly from chronic infections. Limitation of offspring to three or fewer children also is attained mainly at the expense of inducing infection of the genital tract by perversions of the sexual act or induction of abortions.

DR. SITTENFIELD (closing): I wish to thank those members of the Society who have taken an active part in this discussion —I had hoped they would offer a lead for future experimental work in cancer. In answer to Dr. Schmitz's question—whether the repeated hypertrophy of the breast incident to pregnancies in multiparous women do not tend to become a pre-cancerous condition—I would say that we hear far too much about pre-cancerous conditions, without stating in definite terms what constitutes a pre-cancerous condition. Up to the present no one has defined what "pre-cancerous" really means. If we assume that a persistent repetition of hypertrophy or physiological over-activity in a tissue may be responsible for a condition upon which cancer is likely to develop, then we may accept these hypertrophies as causative factors, and these would fall in the line of chronic stimulation.

In my paper I have stressed that chronic irritation, be it external or internal, chemical, physical or thermic, is responsible for a frustrated attempt on the part of the organism to repair repeated injuries.

In the failure to accomplish orderly regenerative repair, the growth-stimulating substances may be held accountable for overgrowth and, ultimately, for transformation of normal into malignant tissue. I have attempted to show that there can be demonstrated in the artificial cultivation of tissue cells a growth-promoting substance and a growth-inhibiting substance, an excess of inhibitory substance probably leading to ulceration and necrosis, and an excess of stimulating substance to irregular overgrowth. If the overgrowth is continuously stimulated by the accelerating substance, it will ultimately lead to malignancy. This process can be repeated over and over again and always with the same result.

Embryonal tissue and cancer tissue exemplify best the presence of growth-stimulating substances. For instance, if kidney or heart tissue is grown in artificial media, it may lie dormant for ten to twelve days, and then begin to grow. If, however, tumor extract or embryonic juice is added to the tissue culture, growth begins at once, *i.e.*, in one or two days. In other words, embryonic tissue extract or tumor extract supplies this growth-promoting substance, which causes growth to occur immediately. This means that the dormant period of ten to twelve days has been wiped out, indicating without any doubt that these juices contain some substances which, when added to tissue cultures, stimulate growth immediately. Just what this substance is, *i.e.*, its physical and chemical nature, has not been analyzed.

To answer Dr. Withers, I am compelled to say that we are at a loss to explain what biological processes are involved in the absorption and reaction in the tissues of primary and secondary radiation.

In answer to another question—whether doses of radium inside and outside of the body act alike—I wish to draw your attention to what I have related to this Society

upon previous occasions. Experimentally it has been shown that when a tumor is excised from the animal and radiated outside of the body, it requires five to seven times an erythema dose to prevent growth upon reinoculation, whereas one and a half to two erythema doses, administered to the tumor inside the animal, will render the tumor non-inoculable. At the same time I wish to state that an erythema dose in a rat is approximately two and a half to three times that of the human skin.

I always strive to avoid an argument with Dr. Slye because I know that she is head and shoulders above me when it comes to the study of heredity in cancer, but still it is very difficult to reconcile facts as we encounter them in the laboratory or to interpret them upon the basis of hereditary factors, be they dominant or recessive. It has been our uniform experience that when we find a spontaneous tumor in an animal, and attempt the first series of inoculations, we are fortunate if we obtain 3 to 5 per cent tumor takes. If, however, this tumor is transplanted through successive generations, say, second, third, and fourth generations, we are able to raise the virulence of that tumor so that it will grow in practically 80 to 100 per cent of the animals inoculated, regardless of what the biological factors of the stock were, whether they were bred in one part of the country or another.

Another example of where this principle of heredity fails us is the fact that the majority of early roentgen operators have succumbed to cancer of the skin. It is extremely difficult to believe that in all these cases there existed a special predisposition to cancer of the skin.

The same applies to experimental tar cancer. Here again the results so far obtained justify the statement that artificially it is possible to produce experimental tar cancers in the large majority of mice. It seems out of the question to me to accept that all these mice in whom cancer was induced by chronic irritation had inherited a specific predisposition, especially when we know that spontaneous cancer of the skin in mice is a comparatively rare occurrence. I regret that this admirable work of Dr. Slye has not been able to explain for me traumatically induced cancers upon the basis of heredity.

MISS SLYE (closing): In the paper I read I tried to draw the distinction as sharply as possible between spontaneous and grafted tumors. Dr. Sittenfield was referring again to grafted tumors, in which he says he can get 100 per cent of takes in almost any animal he selects. That corroborates the very point I was making, namely, that the take of a grafted tumor depends upon the power of the animal to regenerate normally, because it is the cells of the grafted tumor itself which grow and *not the cells of the host.* Naturally, we are going to have—unless we happen to strike cancer stock—pretty nearly 100 per cent of animals which, when irritated and traumatized, are going to regenerate normally and give the proper amount of attachment and food to a parasitic tumor.

In regard to spontaneous cancer arising at the site of single traumas, I have many instances amongst my 5,000 cases of spontaneous malignant neoplasms. To relate one kind of case, which is typical: Careless helpers in the laboratories frequently strike a mouse with the sharp edge of a cage door. What happens? In strains which yield 100 per cent of sarcoma there will, under such conditions, arise a sarcoma at the site of the wound. When this accident happens to an animal with no sarcoma in its ancestry, there has been no instance of sarcoma arising at the site of the wound. Again, where a strain yields 100 per cent of squamous cell carcinoma, either a chronic irritation or a single violent irritation of the skin will form the basis of squamous cell carcinoma.

The whole subject of heredity is a very difficult and complicated one. I am convinced from my own study of it for eighteen years that when we have investigated it thoroughly we shall find that every attribute of organic life is based upon heredity. You will find in your work in therapy that there are certain cases which seem absolutely similar but which show a total dissimilarity of reaction to identical treatment. Why? Because their natural tendencies are different, and each one reacts in accordance with his own identical tendencies.

TECHNICAL AIDS IN THE ROENTGENOLOGIC DEMONSTRATION OF LESIONS HIGH IN THE STOMACH AND ON THE POSTERIOR WALL[1]

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IN the majority of cases, organic lesions of the stomach are demonstrable by simple roentgenologic technics, such as are commonly employed to-day; however, there is a substantial and important minority of lesions which, by reason of their unusual location, require additional minutiæ for their detection, and the roentgenologist should seldom be satisfied with a negative finding if these methods have not been applied. Among the lesions which are most likely to elude observation with the ordinary procedure are those on the posterior wall, and those high in the stomach. As many of you make your own roentgenologic examinations, I have thought it worth while to emphasize certain technical adjuncts which have helped us to demonstrate such lesions, and thus reduce our negative errors to a minimum.

Looking back over the developmental period of gastric roentgenology, it seems to have been extraordinarily fortunate for this method of diagnosis that the two most common diseases of the stomach, ulcer and cancer, most often involve the region of the lesser curvature and produce deformities which can be seen in the dorso-ventral view. Furthermore, since both ulcer and cancer usually occur in the distal half of the stomach, a standing position of the patient is suitable for their demonstration. Thus the erect posture and the dorso-ventral view have become basic features of the roentgenologic examination. It was realized early that lesions remote from the curvatures, or high in the cardia, are a prolific source of error because this region is protected by the thoracic cage and is inaccessible to manipulation. Accordingly, the oblique view, the recumbent position, and palpation over accessible areas were the procedures added to the technic, and are now commonly employed, either routinely or as occasion requires. Yet, even with these methods, a certain percentage of lesions, chiefly those high in the stomach and on the posterior wall, fail of discovery. Although this percentage is not large, it is highly desirable to reduce it if possible, and enhance the exclusion value of negative reports.

Since the majority of gastric ulcers are seen along the lesser curvature, there is a tendency to believe that the ulcers are seated immediately on the curvature. This is not true. As a matter of fact, true "saddle ulcers" are not common; the majority are on the posterior wall, but so near the lesser curvature that the projecting niche is easily seen. With this in mind, the comparative frequency of ulcers on the posterior wall, well away from the curvature, is not surprising. In a series of 639 cases of gastric ulcer, W. J. Mayo found that the ulcer was on the posterior wall, at a considerable distance from the curvature, in 85; and about 75 per cent of these were in the middle third of the stomach, while 16 per cent were in the cardiac third.

It is quite clear that the niche of an ulcer in the upper or middle third of the stomach, remote from the curvature, may not be observed either in the dorso-ventral or oblique view. This applies also to other lesions of the posterior wall, such as ulcerating cancers and benign tumors, which are often small and are likely to occur in this situation. For the demonstration of such lesions we have found a few easily applied technical adjuncts to be of decided value in averting a mistaken diagnosis. These adjuncts are not novel, but their worth is perhaps not sufficiently appreci-

[1] Read before the American Gastro-enterological Association, Atlantic City, April 30-May 1, 1923.

ated. Among them may be enumerated: (1) observation of the contrast meal as it enters the stomach during the process of gastric filling; (2) careful inspection of the sulci between the rugæ when demonstrable; (3) palpatory maneuvers to approximate the anterior and posterior walls of the stomach, and thus reveal a small central filling defect or niche, or elicit abnormalities in the cardia; (4) examination in the Trendelenburg position, and (5) radiography in the oblique or transverse view.

OBSERVATION AS THE STOMACH FILLS

In our early work at the Clinic it was our custom to inspect the esophagus as the first swallows of the barium meal were taken, then wait until the stomach was filled before proceeding with the fluoroscopic examination. By this method we were able to discover lesions along the curvatures, but to our humiliation the surgeons occasionally found an ulcer or newgrowth on the posterior wall which we had overlooked. As one means of obviating these failures, we began to observe the contrast meal as it entered the stomach and note the path which it followed. This seems an almost petty detail, but it has so often averted mistakes that we now never omit it from the routine. Only the first few swallows of the contrast meal need be observed, but inspection must be close, and the examiner must not permit his attention to be distracted to the esophagus or elsewhere.

Under normal conditions the aqueous mixture is projected from the esophagus in a more or less interrupted stream, synchronously with the acts of swallowing. Occasionally the segments are shot across the cardia almost transversely, strike the greater curvature, and then descend into the stomach. In other instances, the stream descends more obliquely and strikes the greater curvature lower down; in still others, it follows the lesser curvature rather closely. Often the stream is not of uniform width, but after leaving the esophagus spreads out slightly in the shape of a fan (Fig. 1*a*). The important point is that, normally, the stream does not wander about haphazardly, but follows a direct course in the upper portion of the stomach, until it impinges on the gastric wall, and then descends as the stomach unfolds before it.

A tumor high on the posterior wall of the stomach usually deflects the whole stream noticeably to either side (Fig. 1*b*), or, if the mass is small, it may cause the stream to divide, part going above, and part below (Fig. 1*c*). The crater of an ulcer or deeply ulcerating cancer in this situation commonly fills, and appears on the screen as a very dense, circumscribed area in the course of the more faintly shadowed barium stream (Fig. 1*d*).

After the stomach is filled, the tumor or ulcer is submerged in the rising tide of barium, and it may be impossible to bring the lesion again into view, either by altering the position of the patient, or by palpatory manipulation. This method, therefore, sometimes offers the only chance of discovering the lesion. When the crater of an ulcer is revealed in this way, the diagnosis is sufficiently established. If there is only a diversion or division of the stream, suggesting a tumor, efforts should be made to confirm its presence by examination in the recumbent, or other postures. But if this confirmation cannot be obtained, and interference with the barium current persists at a second examination, the diagnosis of a lesion is warranted.

If the pylorus is obstructed and the stomach contains much secretion, the barium column, after traversing the gas-bubble, falls through the secretion in blobs which follow no constant path. A similar appearance may be seen if the patient has taken food before examination.

THE RUGÆ OF THE STOMACH

Examiners are familiar with the faint, more or less parallel streaks representing sulci between the rugæ of the stomach. They are noted more often in the vertical middle

portion of an elongated stomach, which is often somewhat narrowed at this point (Fig. 2). In such instances, the presence of the grooves is regarded as evidence that the narrowing is not due to an organic lesion. Aside from this, the mucosal folds and furrows have not received much attention. Recently Eisler and Lenk have given them more serious study. These observers assert that, with a suitable technic, the furrows can be seen in all normal and most of the abnormal cases. The exceptions include dilated stomachs, those with marked hypersecretion, and those with infiltrations of the wall. To visualize the grooves, the patient is given a few swallows of the aqueous barium mixture, and this is distributed thinly over the stomach by stroking palpation. In the region of the gas-bubble, no furrows are seen. Below it, they are visible as far as the pylorus. In the main, they run parallel with each other and with the curvatures, although they may be slightly serpiginous in their course. Along the greater curvature, transverse grooves may be noted, but these are quite short. Since the longitudinal furrows on both walls are visible at the same time, it is difficult to estimate their number, but the average in the pars media seems to be about ten. In certain pathologic cases, usually ulcer of the posterior wall, Eisler and Lenk have noted, besides the parallel furrows, oblique or almost transverse sulci running across the stomach and converging toward a point on the lesser curvature. At this point the niche of an ulcer was commonly, but not always present, and the authors cite a case without a niche, but in which the scar of an ulcer was found at operation.

Quite recently Forssell has made some interesting roentgenologic observations of

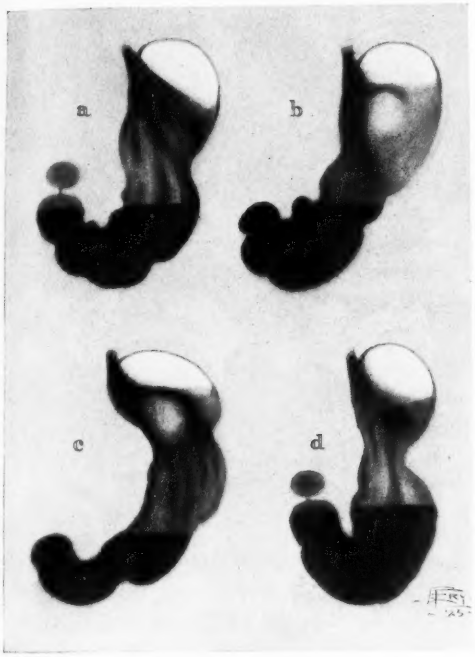

Fig. 1. (*a*) Drawing illustrating barium entering cardia of a normal stomach. (*b*) Barium stream deflected by a tumor high in the cardia. (*c*) Barium stream divided by a tumor high in the stomach. (*d*) Crater of an ulcer on the posterior wall, as seen during the process of filling.

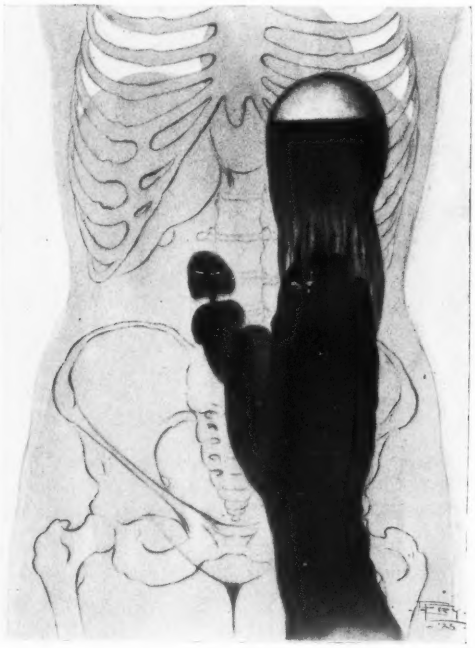

Fig. 2. Drawing showing normal appearance of gastric rugæ during palpation.

the gastric rugæ, from which he concludes that the folds are produced by contractions of the muscularis mucosæ, and not of the muscularis propria, as generally assumed. He finds that in different stomachs, differ-

Fig. 3 (A348157). Perforated gastric ulcer; hour-glass stomach. Note converging rugæ.

ent reliefs of the mucosa are obtained, that the number, position and form of the folds may change in a brief time, and that the anterior and posterior walls of the same stomach may have very different surfaces.

I have observed converging folds only in cases of spastic or organic hour-glass stomach produced by a lesion (Fig. 3). In such instances, the hour-glass constriction is so strikingly indicative of a pathologic condition that convergence of the rugæ is superfluous as an index. In a few cases I have noted normal or perhaps somewhat intensified, parallel sulci with a niche in the course of one furrow. Since the rugæ are obliterated in the immediate area occupied by a tumor (Fig. 4) or the crater of an ulcer, a localized absence of sulci should be regarded with suspicion. On the whole, it would seem that more thorough study of the topography of the posterior wall may prove valuable in various ways.

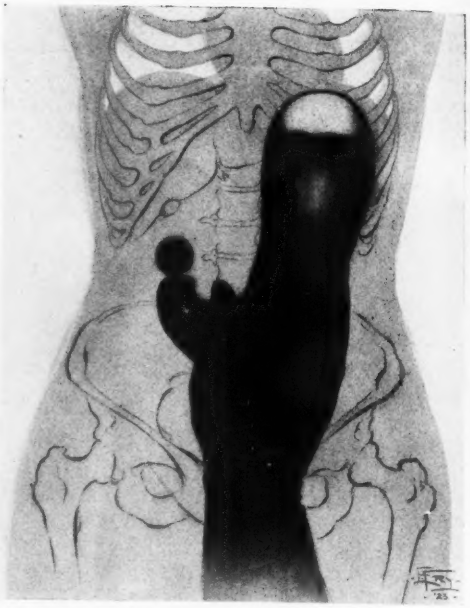

Fig. 4. Rugæ obliterated in the area of a tumor.

PALPATORY APPROXIMATION OF THE WALLS

Palpation during fluoroscopic examination is more or less commonly used to force the ingesta into the cardia or the duodenal bulb, to efface spastic or other artificial filling defects, to discover masses and their correspondence to filling irregularities, and to elicit points which are tender to pressure. Palpatory pressure to bring the anterior and posterior walls near together, thin the opaque ingesta, and thus show abnormalities of the wall, is seldom mentioned. This can be accomplished most conveniently by slow stroking movements of the fingers downward over the stomach during the process of filling (Fig. 2). The latter point is important, for after the stomach is fully distended, it is sometimes difficult to approximate the walls sufficiently to demonstrate small deformities situated internal to the curvatures. This is especially true of stout persons with excessive omental fat and thick abdominal walls which hinder effective palpation.

During this manipulation, tumors on the posterior wall appear on the screen as

Fig. 5 (A396304). Roentgenogram made of patient in the usual anteroposterior position. No crater of ulcer seen (Fig. 6).

translucent areas within the gastric silhouette, corresponding in size and shape to the growth. The excavation of an ulcer appears as a dense spot, usually circular in form, and by turning the patient so as to obtain an oblique or transverse view, a projecting niche may be disclosed. When the walls are approximated as described, an ulcerating cancer usually shows a central opacity, representing the barium-filled excavation, within an encircling translucency corresponding to the surrounding margin, and, outside this, the diffuse density of barium in the stomach. As a rule, the concavity of an ulcerating cancer does not extend into or beyond the gastric wall, so that there is no projecting niche at any angle of view. Absence of a niche and the presence of the three shadow-zones are virtually pathognomonic of this condition.

The value of palpation during fluoroscopy cannot be emphasized too strongly. It is absolutely indispensable, and the examiner who fails to employ it will miss many diagnoses.

TRENDELENBURG POSITION

It is seldom difficult to detect large tumors in the cardia. They may be shadowed within the transparent air-bubble. If not, the barium may be forced high into the

Fig. 6. Same as Fig. 5. Extreme, oblique, transverse view. Crater of ulcer seen high in stomach.

cardia by manual pressure over the stomach, and a filling defect thus revealed; or a trochoscopic examination, with the patient prone or supine, may be decisive. But these measures occasionally fail to show ulcers or small tumors on the posterior wall of the cardia. As I have said, a tumor may split the inflowing stream of barium, or the cavity of an ulcer may show as a deeper opacity at this time, but these phenomena are not constant.

Employment of the Trendelenburg position during roentgenoscopy to examine the cardia is seldom mentioned except by Continental roentgenologists, and by them only occasionally. That it will succeed when other postures fail, I can freely affirm from experience, and I have quite recently had a striking example.

The first examination, with the patient standing, was unsatisfactory because of his acute symptoms, which gave him great distress and caused marked rigidity of the abdominal wall. At a second examination the following day, after giving belladonna, the peculiar way in which the barium accumulated intermittently in the cardia as it entered, suggested the possibility of a high lesion, and the patient was then screened in the horizontal position. Ordinarily, in this position, the barium mixture flows into the cardia and fills it completely. In this case the cardia was poorly filled, and I suspected a niche on the posterior wall near the lesser curvature, but could not be positive. At a third examination the patient was again screened on the horizontal table, but with his hips elevated, approximating the Trendelenburg position. In this posture the cardia was outlined more definitely, and a niche was clearly depicted on the posterior wall. At operation a perforated ulcer, high on the posterior wall of the stomach, was found.

RADIOGRAPHY AT VARIOUS ANGLES

Although the examiner rarely omits the oblique views in roentgenoscopy, he is inclined to forget that plates made in the oblique diameters may also be helpful. Sometimes during the screen examination, he is uncertain whether the gastric margins as seen at an angle, and necessarily from a greater distance, are smooth or not. In such instances, plates made at this angle may reveal a small but definite lesion (Figs. 5 and 6).

As Stierlin, Assmann, and others point out, the assumption is too common that roentgenography in the transverse diameter cannot give a sharp picture because the stomach is too far from the plate. In former days this objection was perhaps valid, but, with the newer apparatus and with the left side to the plate, a roentgenogram can be obtained that will show the anterior and posterior contours of the upper half of the stomach with fair definition. In this position, of course, the lower portion of the gastric outline is overlapped by the shadow of the antrum and duodenum, especially if the stomach is of fishhook form, so that an apparent deformity in this region must be judged with caution.

It is desirable, of course, that technics be simple, but they must be efficient, for there is constantly an increasing dependence on the roentgen ray, not only to expose organic disease of the stomach, but to exclude it. Progress in roentgenologic diagnosis has been due to two factors: first, improvements in the details of examination, and, second, growth in the knowledge of interpretation. Of late years, greater stress has been laid on interpretation, and properly so, for there was much to learn in this respect. Now that proficiency in reading roentgenologic signs has become general, it behooves us again to be on the alert for better methods of eliciting these signs.

The accessory measures which I have mentioned are not hard to apply, nor do they add unduly to the time required for examination. On the contrary they are easily employed, and require but a few moments. That they will forestall many disappointments in roentgenologic diagnosis I am quite sure.

While the X-ray has been of great help to the internists and surgeons of the Clinic, the surgeons in turn have been of great help to the X-ray, not only by confirming its findings and proving the value of roentgenologic signs, but also by revealing lesions that we had not suspected. The latter service has been largely responsible for the technical modifications here described.

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Cardiac measurements.—The work presented represents an effort to establish a closer standard of heart size with body measurements in normal subjects as a basis for practical use in clinical medicine. It involves the introduction of two paramount considerations: first, the use of a series of normal cases most carefully selected on the basis of the usual clinical and special cardiological methods of examination, and second, the application of statistical methods to the study of the data obtained. The factors studied were the heart rate, sitting height, stature, body weight, and age.

New tables are given for the estimation of normal cardiac area in man. These are derived from the formula: Area in sq. cm. = Age 0.0204 + Stature 0.8668 + Weight 0.337 — the constant 63.8049. If the heart is found to be 7 sq. cm. larger than the predicted area, chances are 3 to 1 that it is actually enlarged. With 14 sq. cm. the chances of pathology are 10 to 1, and with 21 sq. cm., 45 to 1.

J. D. Camp, M.D.

Estimation of Cardiac Area in Man. P. C. Hodges and J. A. E. Eyster. Am. Jour. Roentgenol. and Rad. Ther., Sept., 1924, p. 252.

Cancer—palliation and five-year cures.—It is our duty to recognize cancer in its earliest stages and to remove it surgically in the best way known to us if it is still in the primary stage and surgically removable. Where surgery has no chance to remove a cancer completely, there is no excuse for operating.

In cancer of the cervix, the figures of Martzloff and J. G. Clark are compared; Martzloff reported 387 cases, of which only 178 were treated, with an immediate mortality of 14 per cent and 10 per cent of five-year cures. Clark reported 144 cases, all of which were treated (radiation),—no immediate mortality and 10 per cent of five-year cures. Martzloff had 209 cases which were inoperable and beyond surgical palliation; Clark's cases all received palliation and 10 per cent were cures. Yet Clark says not to talk too loudly about cures, because the palliation would, alone, justify radiation.

In breast cancer, this author regards as inoperable a carcinoma in which one or more of the following factors exist: fixation of tumor to chest wall; involvement of supraclavicular nodes; definite involvement of opposite axillary nodes; diffuse subcutaneous nodules; diffuse inflammatory carcinoma involving considerable skin area; chest metastases; more remote metastases. No palliation is to be expected from surgery in these cases, but radiation will prolong life and ameliorate symptoms. Ewing is quoted as saying that breast cancer never comes untouched to autopsy, surgical enthusiasm always preventing this.

W. W. Watkins, M.D.

Palliation in Cancer of the Uterine Cervix and Cancer of the Breast. Edgar A. Ill. Jour. Med. Soc. of N. J., Aug., 1924, p. 243.

Radiotherapy of ovaries.—Treatment is based on the principle that on stopping the function of the ovaries, menstruation will cease, and the disturbances—such as metrorrhagia, menorrhagia, dysmenorrhea and uterine fibroids—which are associated with perverted ovarian function or abnormal menstruation, will cease. In the latter condition, if young women are treated, a temporary castration is produced and during the amenorrheic period, the tumor may retrogress. In women over forty, permanent castration is the treatment.

Technic of Seitz and Wintz is advocated of giving to each ovary 34 per cent of the skin erythema dose, at one sitting. The author uses 215 KV., 4 ma., 50 cm. distance, ¾ mm. copper and 1 mm. aluminum, portal of entry 20x20 cm., front and back, average total time of two hours. He has never found it necessary to repeat this dosage.

W. W. Watkins, M.D.

Roentgen-ray Therapy in Hemorrhagic Metropathies and Uterine Myomata. Jacob Roemer. Jour. Med. Soc. of N. J., Aug., 1924, p. 249.

RADIO-ACTIVE SUBSTANCES AND THEIR THERAPEUTIC USES AND APPLICATIONS

RADIO-ACTIVITY

By JOSEPH MUIR, M.D., NEW YORK

THE present article is an introduction to a series of articles dealing with the therapeutic uses of radio-active substances. No theories will be advanced in this article: the conceptions of the atom and rays given are the ones generally admitted and borne out by the references.

All definitions and facts stated are presented without delving deeply into theoretical considerations, and are intended only to give a general idea of the subject to the users of radio-active substances for therapeutic purposes, so that the articles to follow may be fully understood.

To study radio-activity, it is necessary to take up in some detail the generally accepted conceptions of the atom: its structure and general physical properties. We are all familiar with the grouping and arranging of the so-called chemical elements into a table called the Periodic Table of Mendeleeff. A survey of this table and a close study of each of its groups, and, in particular, of each element in each group, reveals very uniform connections existing among the atoms of the various elements. Due to these connections, it has been universally accepted that the atoms of the elements are not different in nature, but very similarly constituted and made up of identical units. This point of view entirely does away with the old idea that an atom is the simplest and indivisible form of matter.

In the following dissertation, an all-important position is occupied by negative electricity and its occurrence as such, that is, as particles of electricity or pure atoms of negative electricity. Such particles are called electrons and have mass and inertia. The mass of an electron or electronic mass is of very small magnitude compared to that of ordinary atoms and ions. The mass of a hydrogen atom, the atom of smallest mass, is 1,800 times greater than the electronic mass.

There are many proofs for the existence of the electron, and let it suffice in this connection to state that the specific charge of the electron, the ratio of the elementary charge e of the electron to the electronic mass m, is 1.769×10^7. This value has been obtained in many different ways; namely, cathode rays researches, optical experiments, measurements of spectral lines, etc., and the values obtained check within limits of error.

We see the electron associated with matter, and we can see it at work as is the case in the conduction of an electric current along metals, the production of roentgen rays, etc. The electron has been considered as the universal element of the structure of all matter and it is with this idea in mind that we study the atom of the chemical elements.

The atomic number of an element is a number which gives the position of the element in the Periodic Table. The atomic weights of the elements are integral numbers when they are referred to oxygen as 16; and the atomic number of an element does not coincide with its atomic weight, but with half the atomic weight. The atom will now be considered in the light of electrical charges.

Experiments with cathode rays, and the laws connected with the absorption of these rays, have revealed the fact that matter has a perforated structure and only a small part of it is impenetrable by cathode rays. This same revelation has come from experiments on alpha-ray scattering.

When an alpha ray penetrates matter it is bent sharply. This sharp bending is caused by very intense electric fields, which

in turn are caused by a charge in an atom. That charge is concentrated in a very small element of space called the nucleus. The electric field associated with the atom, causing the deflection of the alpha particle, is called the deflecting field; the atom being of the deflecting element.

The magnitudes of the deflections may be measured. It has been found that by changing the deflecting element the deflection increases with the atomic weight of the deflecting element; hence, the deflecting field must also increase with the atomic weight. This field can be considered produced by a point charge which obeys Coulomb's law of electrical attraction, and having measured the magnitude of the deflections we can calculate the magnitude of the charge that the nucleus of the atom of the deflecting element must have to account for the observed deflections.

Experiments have been carried out and checked values have been obtained of the charges that correspond to different nuclei. These values are given as multiples of the elementary charge e, and their numerical value agrees within limits of error with the position of their corresponding elements in the periodic system; namely, the atomic number. The charge of the nucleus, or nuclear charge, is then equal to the atomic number numerically.

The alpha particle being positively charged, the nuclear charge may cause the bending of the particle by either attraction or repulsion, depending upon the sign of the nuclear charge. However, to bring about the noted deflections, the nucleus must have resistivity and must, of necessity, be positively charged to possess the necessary resistivity. Therefore, the positively charged alpha particle is repelled by a positively charged nucleus when it passes very close to the latter.

An atom of any element must be a neutral body electrically. Since the nucleus is positively charged, there must be in the atom, aside from the nucleus, particles of negative electricity, electrons, sufficient to neutralize the positive charge of the nucleus. The positive charge, or nuclear charge, is equal to the atomic number times the electronic charge e; therefore, the atomic number must be equal to the number of electrons around the nucleus. Hence, the total number of electrons in an atom is equal to the atomic number of the element. For each element in the Periodic System the nuclear charge grows by one unit and the nuclear mass by two units. Also, each element consists of one more electron than the preceding element.

The electron contributes only a negligible amount of atomic weight, so that the atomic weight is represented by the mass of the nucleus. Alpha-ray observations have permitted deductions as to the size of the nucleus, and it can be, at the most, of sub-atomic size. In the neighborhood of the nucleus, then, there is an atmosphere of electrons which are attracted by the nucleus. The question immediately comes up, how do the electrons maintain their distance from the nucleus?

The only answer given to this question is the assumption that the atom has the general configuration of a solar system. The electrons are the planets and they revolve around the central body, the nucleus. In this planetary scheme the gravitational force expressed by Newton's law is replaced by the electrical attractions expressed by Coulomb's law.

Since it is confusing to visualize such a system let us take an electron around the nucleus and the repulsions acting on it from the other electrons. It is easy to see that the resultant force of all these repulsions has a line of action passing through the nucleus and directly opposes the attraction of the nucleus. By varying the velocity of the electron around the nucleus we arrive at a point where the centrifugal force acting on the electron plus the repulsions from the electrons equal the attraction from the nucleus.

The Simple Atoms

Hydrogen is the lightest of all the elements and is the simplest atom. Its atomic number is unity and the atom itself is formed by a nucleus possessing one positive charge and an electron revolving around this charge or nucleus. The size of the atom must, of course, be determined by the distance of the electron from the nucleus and this, in turn, by the velocity of the electron around the nucleus. This electron is not in close bond with the nucleus. It is free to a certain extent and can be removed from the atom. When the hydrogen atom loses its electron, the system becomes positively charged and the result is the hydrogen ion. It is only a nucleus, positively charged, of very small spacial dimensions, since the electron has been removed. Its size is infinitesimal compared to atomic dimensions.

Helium has an atomic weight of 4, and atomic number 2, therefore it consists of a nucleus carrying two positive charges and two electrons rotating around the nucleus. One of these electrons is in close bond with the nucleus, and the other is free in the same fashion of the electron of the hydrogen atom. When the latter electron is removed from the system, the nucleus exerts a greater attraction on the remaining electron and it is drawn closer to the nucleus. The resulting system is a helium ion, charged positively and having a size much smaller than the helium atom but infinitely larger than the hydrogen ion. In the helium ion there is still one electron rotating around the nucleus, which gives size to the structure.

The Alpha Particle

When the remaining electron in the helium ion is removed the result is the alpha particle. It is a nucleus with two positive charges and without real extension, vanishingly small when compared in size to the hydrogen atom. It is comparable to a hydrogen ion, being just a nucleus.

This doubly positively charged nucleus has great resistivity, and its structure explains its characteristic properties. It has an enormous penetrating power, intruding freely into the planetary systems of other atoms, but being repelled by the nuclei. It is this characteristic which has put in the hands of man an agent by means of which the interior of the atom may be explored and more data obtained on its internal structure.

(To be continued)

Syringomyelia.—The article contains a brief review of the literature concerning the pathology and roentgen treatment of syringomyelia. The observations of one case are reported in detail. Inasmuch as some of the cases are probably due to a neoplastic change, it is thought that they may be affected favorably by roentgen radiation. As roentgen radiation appears to arrest the progress of the disease, and no other form of treatment appears to affect it, the author believes that roentgen radiation is advisable.

J. D. Camp, M.D.

Roentgen-ray Treatment of Syringomyelia: Report of a Case. A. S. Merrill. Am. Jour. Roentgenol. and Rad. Ther., Sept., 1924, p. 214.

RIGHT-SIDED DIVERTICULITIS AND DIVERTICULOSIS[1]

By LEON THEODORE LEWALD, M.D., Professor of Roentgenology, New York University and Bellevue Hospital Medical College

WHEN the term "diverticulitis" is used one almost invariably thinks of a left-sided lesion of the colon. While diverticulitis is more commonly encountered on the left side, we wish to emphasize the fact that the condition is by no means confined to the descending colon and sigmoid. Having recently encountered a number of cases in which severe lesions, including perforation of the colon, complicated diverticulitis of the right side, the importance of its recognition has been impressed upon the writer. Numerous articles have been written on the subject of diverticulitis that neglected to mention the possibility of its occurring on the right side. Dr. John F. Erdmann[2], however, in 1918 reported twenty-seven cases, one of which was in the ascending colon, the remainder being in the sigmoid.

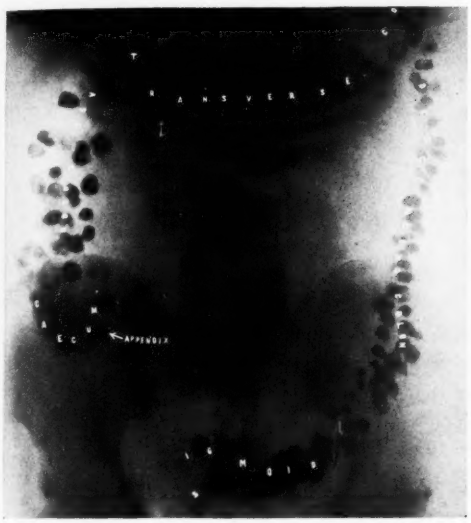


Fig. 1. Diverticulitis and diverticulosis. Note large number of diverticula as far back as the cecum. Twenty-three hours after injection. This patient had an inflammatory attack of diverticulitis on the left side.

It is well to make a distinction between the mere presence of diverticula and "diverticulitis," the term "diverticulosis" being applied to the former condition. The term "diverticulitis" should be used only when there is a complicating inflammation. It is quite possible to have a combination of diverticulosis and diverticulitis; in fact, this is often the case (Fig. 1).

Fig. 2. Right-sided diverticulitis. Clinical diagnosis, chronic appendicitis and cholecystitis. Note spasticity of hepatic flexure and right half of transverse colon, indicative of inflammation in this region (R.U.Q. symptoms). Sixty-nine hours after meal, 8 min. after colon injection. Diverticula remain filled from opaque meal. *One diverticulum was still filled on 52nd day, when examination was discontinued.*

One of the most striking evidences of diverticulitis, from a roentgen standpoint, is the presence of a localized narrowed lumen with spasticity, indicative of surrounding pressure, such as might be caused by an inflammatory exudate. If the opaque injection be given prior to the meal, this narrowing may be the only indication of diverticulitis, for, in my experience, diver-

[1] Read before the Radiological Society of North America, at Chicago, June, 1924.
[2] *Surgery, Gynecology and Obstetrics*, Feb., 1918.

ticula have been more frequently observed after an opaque meal than after an injection. It is my custom to give a meal first in most instances. In cases of multiple diverticula some of the pockets will usually

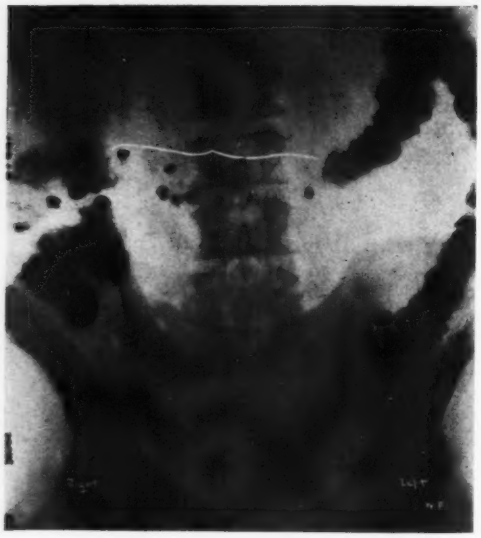


Fig. 3. Right-sided diverticulitis. Note apparent irritability of transverse colon in region of diverticula (R.U.Q. symptoms). Thirty-five min. after colon injection and after partial elimination. *One large diverticulum in region of hepatic flexure remained filled on the 98th day.*

remain filled at the end of two or three days (and often much longer), even after catharsis as a preparation for injection. If the colon is now injected it may be observed that in the region of some of these diverticula, which have remained filled from the opaque meal, there is a filling defect in the colon suggestive of irritability (Figs. 2 and 3). On several occasions, in cases of multiple diverticula, such a filling defect has been observed in the exact region where the patient complains of pain and where a tender mass may be palpable. Hence, it is possible that this area of apparent irritability might help to locate a diverticulitis when there are multiple diverticula present. This lack of filling associated with irritability differs from a filling defect due to newgrowth in that the former is not constant and is not obstructive. It resembles more the roentgen appearance of an ulcerative lesion of the colon such as tuberculosis, where the most characteristic finding is a spasmodic filling defect due to irritability of the inflamed mucosa.

Case[3] has called attention to the fact that a diverticulum of the colon may retain the opaque substance for a number of days and refers to a case of the author's in which there was retention for ten days. We have recently had two cases, in one of which there was a retention for *fifty-two days* (examination discontinued) (refer to Fig. 2), and in the other for *ninety-eight days* (refer to Fig. 3). The tendency for prolonged retention in a diverticulum of the gastro-intestinal tract is of value in the differential diagnosis from ulcer. This is particularly true in the upper digestive tract. In two cases we have observed retention in a diverticulum of the stomach twenty-four hours after the opaque meal, whereas in ulcer of the stomach we have not observed retention in the crater after elimination of the meal from the stomach. In diverticula of the duodenum we have observed retention twenty-two hours after the opaque meal.

It is noteworthy that the presence of diverticula has been observed in different regions of the digestive tract of the *same* individual in a number of instances. In one case a diverticulum of the cardiac end of the *stomach* was associated with diverticula of the duodenum, jejunum and right side of colon (Figs. 4 and 5). In another instance there was a combination of a large diverticulum of the duodenum and multiple diverticula of right and left sides of the colon, one of which remained filled for twelve days (Figs. 6 and 7). In a third case there was a diverticulum of the middle third of the esophagus, associated with multiple diverticula of the right side of the colon (Figs. 8 and 9).

[3] Bulletin, Battle Creek Sanitarium, July, 1924.

Fig. 4. Two diverticula in right half of colon. Forty-six hours after opaque meal. Diverticula of stomach and jejunum in same case shown in Figure 5. There were also two diverticula in the duodenum.

Fig. 5. Diverticula of stomach and jejunum. The duodenum also showed two diverticula (confirmed at operation). For diverticula of right side of colon in *same* individual, see Figure 4.

It is a well-recognized fact that the clinical symptoms of subacute diverticulitis associated with an inflammatory mass may be confused with those of carcinoma of the colon. I should like to refer to three cases in particular: one, a male, aged 47, who was referred for roentgen examination because of right-sided abdominal pain. A diagnosis of appendicitis had been made several times during the four preceding years. Roentgen examination revealed the presence of at least one diverticulum in the region of the ascending colon and the presence of a number of diverticula in the descending colon. The appendix was sluggish and retained traces of the opaque substance for several days. A diagnosis of multiple diverticula of the colon was made. The patient was treated by means of colonic irrigations and catharsis and remained free from subsequent attack until about one year later, when he was confined to bed with a severe attack of pain on right side, upper quadrant. At this time a distinct mass could be made out in the ascending colon in the region where a diverticulum had been noted at the previous roentgen examination. There was no tenderness in the region of the appendix. Roentgen examination at this time showed evidence of spasm and incomplete filling of the ascending colon in the region of the palpable mass. The appearance was not suggestive of newgrowth and in view of the previous evidence of a diverticulum in this region a roentgen diagnosis of diverticulitis was made. A third examination after an interval of a month, during which time the patient had recovered from the severe attack, with a disappearance of the palpable mass, showed no filling defect of the colon. The case was evidently one of right-sided diverticulitis.

To emphasize the importance of the findings in the above case, two similar cases are reported, even though the lesions were on the left side.

The first, a woman, aged 63, who com-

Fig. 6. Diverticula on both right and left sides of colon. Ninety-six hours after opaque meal. See Figure 7 for large diverticulum of duodenum in same individual.

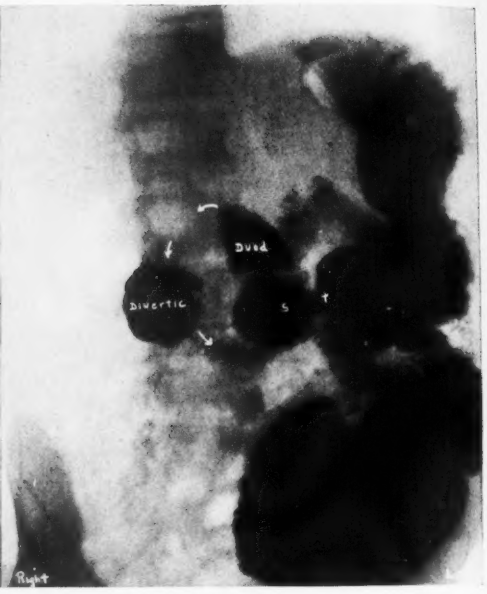


Fig. 7. Diverticulum of second portion of duodenum. For right-sided diverticulum of colon in *same* case, see Figure 6.

plained of an indefinite left-sided distress. A colostomy with excision of a portion of the pelvic colon had been performed twelve years previously following a puzzling abdominal condition of ten days' duration. Before the operation the patient was informed she had a malignancy of the colon. Examination of the specimen showed no evidence of malignancy. A roentgen examination twelve years after the colostomy showed the presence of diverticula in the transverse colon, splenic flexure and descending colon. *There was no evidence of malignancy.* The patient desired to have the colostomy closed, but this appeared impossible because of the large amount of pelvic colon that had been removed.

In the second case, referred to the writer and later reported in detail by Dr. Robert Abbe[4], a clinical diagnosis of carcinoma had been made and X-ray examination requested simply to show the extent of the lesion. Roentgen examination showed definite evidence of diverticulitis and *no evidence of carcinoma* and was so reported. Operation confirmed the X-ray findings. This case is credited as being the first in which a differential diagnosis between carcinoma and diverticulitis was made roentgenographically.[5]

Since it is not easy to differentiate clinically between right-sided diverticulitis, cholecystitis or appendicitis, roentgen examination may solve the problem by demonstrating the presence of diverticula on the right side. These diverticula might be located in the cecum or ascending colon (Figs. 1, 6, 8), hepatic flexure (Figs. 1, 2, 3, 4, 8), right half of the transverse colon (Figs. 1, 2, 3, 10), or in a loop of sigmoid passing to the right of the midline (Fig. 11). When, in addition to the presence of diverticula, there is roentgen evidence of appendicitis or biliary calculi, an operation may be necessary to decide which is causing the patient's symptoms. If the diverticula are found to be uninflamed, they may be inverted and sutured (Fig. 10).

[4]Abbe, R.: A Case of Sigmoid Diverticulitis Simulating Malignancy. *Med. Record*, Aug. 1, 1914, pp. 190-191.

[5]Carman, R. D.: The Roentgen Diagnosis of Diseases of the Alimentary Canal. Second edition, p. 547.

Also Case, J. T.: Personal communication May 18, 1920; also George, A. W.: Personal communication May 10, 1920, correcting error in paper entitled "Use of X-ray in Study of Diverticulitis."

Fig. 8. Two diverticula in right half of colon. Ninety-five hours after opaque meal. Figure 9 shows a large diverticulum of the esophagus in the *same* case.

Fig. 9. Diverticulum of middle third of esophagus. For diverticula of right side of colon, see Figure 8.

A *transposition* of the viscera would produce a diverticulitis of the *sigmoid on the right side.*

If perforation of a diverticulum on the right side occur it might lead to an erroneous diagnosis of appendicitis. On the occurrence of acute inflammatory symptoms on the right side in a patient whose appendix had been removed a number of years previously, we were able to make a diagnosis of perforation of a diverticulum on the right side, because of the fact that a roentgen examination several months before showed the presence of diverticula in this region. Perforation occurred in spite of the fact that diverticula on the right side were filled by bismuth taken medicinally, as shown roentgenographically. Pus was evacuated through an abdominal incision. A fecal fistula persisted for a number of months and finally closed, with apparently complete recovery of the patient.

A radiograph prior to the administration of an opaque meal is at times essential in distinguishing a diverticulum from a smooth foreign body, such as a gold cap, lodged in the digestive tract.

CONCLUSIONS

1. It is necessary to add *diverticulitis* to the list of lesions ordinarily encountered on the *right* side of the abdomen.
2. The term "diverticulosis" should be used to denote the presence of diverticula unassociated with any inflammatory process.
3. Diverticula of the colon are not infrequently associated with diverticula of other portions of the digestive tract.
4. Diverticulitis may at times be manifested by the evidence of irritability of the colon, with *or without actual filling of diverticula.*
5. Diverticulitis may be differentiated from carcinoma of the colon by careful roentgen study.

DISCUSSION

DR. LEWALD: In this case, which I had some time ago, it struck me that with the

presence of the numerous diverticula on the right side one might become inflamed, and yet in this instance the patient had only one inflammatory attack and that was on the left side. He has just died, about ten years after this examination, during which time

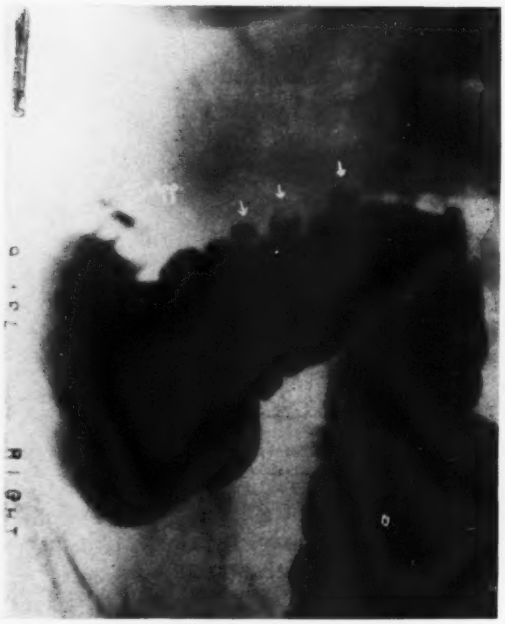


Fig. 10. Diverticulosis of right side of colon associated with chronic appendicitis with inverted appendix. At operation appendix was removed and diverticula inverted, purse-string suture being placed about the base of each.

he has had no subsequent attack, but it is one of the best examples of the presence of diverticula extending all the way from the cecum to the rectum.

A MEMBER: Is that diverticulosis or diverticulitis?

DR. LEWALD: This is a combination of diverticulitis on the left side with diverticulosis throughout the rest of the colon.

DR. G. E. PFAHLER (Philadelphia): I am very much interested in this subject, because the last case that I reported on before I left my office was that of a woman who had had her gall bladder removed and her appendix removed for pain on the right

Fig. 11. Diverticula in sigmoid flexure which injection of colon showed passed to *right* of the midline. *Twenty-two days after opaque meal.*

side, and the pains continued, and I found three diverticula near the gall-bladder region and another diverticulum down at the appendix, without any other diverticula just in that localized region. I have seen a number of these right-sided diverticula, and I supposed that they were looked for in general on that side, because I have certainly seen, as Dr. LeWald has shown, diverticula in every part of the colon.

ROENTGENOLOGIC FINDINGS IN A CASE OF PHYTOBEZOAR[1]

By W. O. UPSON, M.D., Battle Creek Sanitarium, BATTLE CREEK, MICHIGAN

THE term "phytobezoar" is applied to a mass found in the stomach or intestines, composed of food materials, such as skins and fibers of fruit, colloid portions of vegetables, and starch granules, with an occasional small amount of other organic material, frequently surrounding fruit seeds. The process by which these food balls are formed is not definitely understood, but it is probable that the gum and pectin contained in the persimmon and other fruit, combined with the muscular activity of the stomach, can be considered as a more or less direct cause. It is generally considered that the formation of the food ball occurs at one particular time, possibly within a few hours after the ingestion of a quantity of fruit, very often the persimmon. However, it is not unreasonable to suppose that more material may be added, and the bezoar be gradually increased in size.

The usual clinical picture is that of acute gastritis occurring immediately or within a few hours after the ingestion of the fruit.

Fig. 1. Stomach, patient erect, film anterior, immediately after ingestion of meal. Note indefinite rounded filling defect due to bezoar, displaced into the antrum.

Fig. 2. Roentgenogram 2½ hours p.c. Bezoar is easily made out by streaks of barium clinging to it.

In the eight cases reported recently by Hart, seven presented acute symptoms of indigestion; in the eighth case the gastric symptoms were chronic, extending over a considerable period of time. After medical treatment in which hydrochloric acid was administered, small masses were passed in the feces, which contained apparently prunes, bits of raisin skins and stems, and vegetable detritus. Following the treatment, the tumor that had been previ-

[1] Read before the Radiological Society of North America, at Chicago, June, 1924.

ously noticed in the epigastrium disappeared, and the symptoms subsided.

The case which we wish to report gave a similar chronic history. Mr. W., age 42, occupation, farmer. The patient applied for examination and treatment of some gastric disturbance. The present trouble began four or five years ago. No idea was offered as to the cause. The distress began as a heavy sensation in the region of the stomach, sometimes in the throat, coming on three or four hours after meals. This was not a constant affair, but occurred about once a week. Since then it has gradually increased in frequency and in severity so that, for the past few months, the patient has had a gnawing, burning pain in the region of the stomach three or four hours after meals, attended by more or less belching of gas, and sour stomach. This distress was always relieved by the intake of food. Sodium-bicarbonate had not been tried. The patient never vomited any blood or passed any black, tarry stools so far as he knows. Always a fairly hearty and rapid eater, and fond of highly seasoned foods. The patient has, nevertheless, been regular about his meals.

Fig. 3. Film made 4½ hours p.c., showing displacement of bezoar into the fundus.

Fig. 4. Photograph of the bezoar after removal.

The barium-meal study revealed a decided thinning out of the barium in about the middle portion of the stomach. This area measured two and a half to three inches in diameter, and it was found on manipulation that this apparent mass could easily be made to change its position; it being possible to move it to any desired point in the stomach from cardia to pylorus. It did not interfere with the normal peristalsis and there was no evidence of pyloric obstruction. (See Figs. 1, 2 and 3.) At the four-and-a-half-hour observation only a trace of barium remained in the stomach. From the roentgenological findings a free tumor in the stomach was diagnosed.

Dr. Case performed a gastrotomy, through a left trans-rectus incision. A foreign body, the size of a hen's egg, was found free in the stomach. It seemed to be very hard. A small opening was made into the stomach to remove this foreign body. The patient made an uneventful recovery and in about two weeks left the hospital.

The foreign body removed proved to be a bezoar (Figs. 4 and 5), oval in shape, measuring about two inches in its greatest diameter. It was black on the outside and

Fig. 5. The bezoar split, showing its structure.

brown throughout a section. In places there were scale-like layers as large as one's thumb nail that looked like fruit slices. Some of the material resembled tobacco leaves (the patient was an inveterate chewer of tobacco). Microscopically the mass consisted of practically nothing but cellulose in the form of layers of vegetable cells, and in the very center, a persimmon seed, according to Dr. Francis Carter Wood, who kindly studied the specimen. Comparing these with a thin section of cork, they were almost identical. The material, on drying and burning, left very little ash, showing that it was all organic material.

Radiation treatment of laryngeal carcinoma.—Intrinsic laryngeal carcinoma may be roughly divided into two groups of cases, mainly from the standpoint of the ease of spread and the resulting prognosis: (1) Those in which the lesion arises in the anterior portion, where the cartilage affords an adequate barrier against spread through it for a time, and lymphatic drainage is very poor; (2) those cases in which the growth lies more posteriorly and where lymphatic drainage is quite free, allowing the lesion to spread more readily. Growths in the anterior portion can be regarded as distinctly localized lesions for a comparatively long period, and they should offer excellent opportunities for radiation treatment if this could be applied in an adequate manner. Many such lesions disappear in a very satisfactory manner only to recur hopelessly. The difficulty lies in the inability to radiate properly the entire involved area and the giving an excessive dose is prevented because of the anatomical characteristics of the laryngeal structures. Subsequent operation in several primarily successful instances showed an extensive lesion below the cords, part of which was beyond the range of vision and adequate radiation. This undestroyed portion below the cords has undoubtedly been the most frequent starting point of recurrences. Post-operative radiation is strongly recommended by some operators, but its efficacy must remain a matter of doubt for the time being. In extensive growths posterior and extrinsic, palliative radiation after tracheotomy is practically the only procedure to be considered, except tracheotomy alone. Large doses should not be given as they can accomplish no permanent good and only add to the discomfort of the patient.

After a trial over a period of many years the author has found the results of radiation treatment of laryngeal carcinoma to be very disappointing, and the superiority of improved surgical technic in operable cases is freely acknowledged.

J. D. CAMP, M.D.

Some Observations on the Radiation Treatment of Carcinoma of the Larynx. H. K. Pancoast. Am. Jour. Roentgenol. and Rad. Ther., Sept., 1924, p. 217.

Technic for treatment of neoplasms.—The author believes that it is better and more economical to attempt the treatment of the first centimeter of tumor tissue with a lower voltage (100 KV.), and each successive centimeter with different voltages and different filters, in the belief that the rays of the low voltage are absorbed in the first centimeter of the neoplasm and few reach the deeper areas of the tumor, the more penetrating rays going through the superficial cells and being absorbed by the deeper cells. It is believed that rays can be delivered in many different ways so that they may be absorbed at the desired depth. The author is of the opinion that many lesions will receive more benefit and heal more quickly where both radium and the roentgen ray are used, with a variation of the filter and voltage, than where each is used alone with moderate or heavy filtration.

J. D. CAMP, M.D.

Mixed Radiation in Malignant Disease. D. Y. Keith. Am. Jour. Roentgenol. and Rad. Ther., July, 1924, p. 53.

ADVANCED TROUBLE SHOOTING

"The Coolidge Circuit"

By C. B. HORSLEY, Pittsburgh, Penna.

IT might well be said that fully 50 per cent of all trouble experienced with the modern X-ray apparatus is caused by loose connections or short circuits in the Coolidge circuit. Because of the low voltage used to excite the filament and also because a very small variation in the amperage passing through the filament will produce a comparatively great change in the milliamperage through the tube, trouble here might well be anticipated.

It very often happens that a variation in the milliamperage is taken at once to indicate a variation in the line voltage and a separate line is brought in at great trouble and expense, only for it to eventually turn out that a loose reel was the cause of the trouble.

When an excessive variation in the milliamperage first appears, the first step is to tighten all the connections on the cathode connector, the connection at the reels, etc. If this does not seem to relieve the trouble, light the filament and heat it up to a temperature that would give approximately its full milliamperage rating at a five-inch parallel spark gap under normal conditions. Do not energize the tube, but allow the filament light to remain on. At the end of several minutes and while the filament is still lighted, go over the entire Coolidge circuit, feeling each joint and connection. Pay particular attention to the reels at their hubs and also where the reel wires are connected to the cathode connector. That part or joint which feels warmer than the rest of the equipment is the seat of the trouble. Once the trouble is properly located its remedy is only the matter of tightening a connection, or perhaps renewing a reel. It is not unusual to find upon wiping the oil from the hub of a reel that the trouble miraculously disappears.

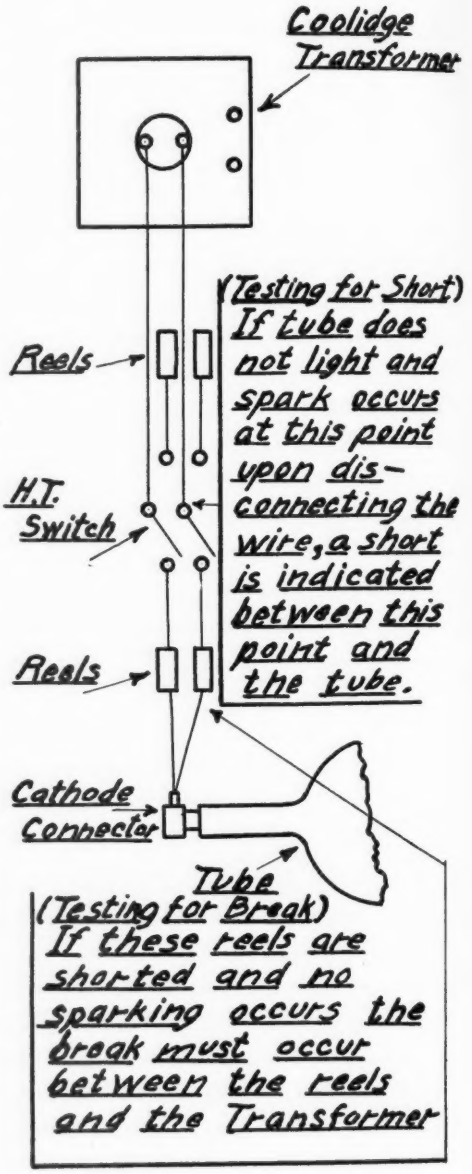


Figure 1

Often, however, the trouble is not that the milliamperage varies, but that the filament does not light at all. In the preceding article[1] the problem of testing the filament transformer was dealt with. If the filament transformer is furnishing current at its secondary terminals and the tube does not light, first see that the cathode connector is tight and that the high tension switch is in correct position. If the tube still does not light, test the two reel wires for a spark by touching the terminals together. By testing for a spark at different stages along the circuit the break in the circuit may finally be run down. If the trouble appears to be a short, rather than a break in the circuit, the short may be segregated by disconnecting the circuit at different points and testing for a spark (Fig. 1).

If no current is reaching the filament transformer and if by the use of a test lamp it is seen that the break is in the filament control, the control unit should be disconnected and removed to a table or bench where sufficient light may be had before any attempt to repair the apparatus is made.

[1]See *Radiology*, Dec., 1924, p. 502.

Effect of irradiation upon chronic myelogenous leukemia.—1. Of 166 patients with chronic myelogenous leukemia, 78 treated by irradiation and 52 not so treated are known to be dead. The latter serve as a control group to the former.

2. The disease is most frequent at from 35 to 44 years of age. Below 25 the disease is rare.

3. About 60 per cent of cases of chronic myelogenous leukemia occur in males, and 40 per cent in females.

4. The insidious onset of the disease makes early diagnosis difficult. The length of time between the appearance of symptoms and diagnosis was on the average 1.4 years for 148 cases.

5. Irradiation has had little effect on prolonging the life of these patients. The early institution of irradiation as yet does not promise an important increase of life expectancy. The average duration of life after the first symptom of the disease in 52 non-irradiated cases was 3.04 years, and in 78 irradiated patients 3.5 years. Of these 130 patients, 42 per cent lived from two to four years, and 12 per cent more than five, and up to ten years.

6. Continued properly administered irradiation produces symptomatic relief, which is often marked and offers to the patient the best guarantee of the longest possible preservation of his working capacity. As the disease progresses, efficiency decreases in spite of continued therapy.

7. All but 5 per cent of the 78 patients were benefited sufficiently by radium or roentgen ray to remain able and useful for varying periods of time. At least 50 per cent became temporarily symptomatically well. This is in contrast to the fact that but 6 per cent of the 52 non-irradiated patients had moderate remissions.

8. The duration of efficient life as compared to the length of life after diagnosis or beginning irradiation, either early or late, shows that on the average it is at least 30 per cent longer in irradiated patients. This percentage time of useful and able existence and the degree of efficiency are both much greater when treatment is begun before than after the middle of the disease.

9. The actual duration of useful life (average 1.6 years for 78 patients) after the first irradiation is proportional to the duration of the disease.

10. The statistics given enable one to forecast the probabilities of the duration of life and the general ability of the patient with chronic myelogenous leukemia.

SOLOMON FINEMAN, M.D.

Chronic Myelogenous Leukemia: Age Incidence, Duration, and Benefit Derived from Irradiation. George R. Minot, Thomas E. Buckman, and Raphael Isaacs. Jour. A. M. A., May 10, 1924, p. 1489.

CASE REPORTS AND NEW DEVICES

TWO GRATIFYING RESULTS

By S. C. BARROW, M.D., SHREVEPORT, LA.

Case I. Mrs. H., aged about 70 years. Thirteen years ago, in a foolish effort to remove superfluous hairs from the face, this patient received a severe X-ray burn, which during all this time has resisted every method used in an effort to secure healing.

Fig. 1, Case I.

In January, 1924, she came to the writer's office showing a large ulcerated area with infiltrated edges, presenting irregular areas of epithelial proliferation, the whole aspect being one of malignancy, irregularly distributed in the ulcerated area. The condition throughout all this time had been very painful to the patient as well as to the writer, who administered the original treatment in the days of coils, gas tubes and interrupters. Throughout the whole time, however, she had remained loyal and unresentful and had given us every opportunity for administering what treatment we could think of, as being indicated, all of which had been of no avail.

In January we began the use of ultra-violet radiation with the air-cooled lamp, administering a dose sufficient to produce a hyperemia over the whole of the side of the face, which was repeated from three to four or five times per week. At the same time extremely gentle doses of unfiltered radium applications were applied about once weekly to the elevated proliferating islands of tissue. After three months' time the sore had completely healed, leaving a smooth, soft, pliable scar, with all pain relieved.

It is needless to say the patient is very happy, likewise her physician.

Case II. Mr. R., aged 80 years. Referred by Dr. P'Pool of Nacogdoches, Texas. Thirty years ago this patient had the right eye removed for cancer—so described by him. At this time he presents himself with large epitheliomas, each about the size of a twenty-five-cent piece, on the neck near the angle of each jaw, and a newgrowth on the left eye occupying the outer half of the cornea from near the edge of the pupil, extending back towards the outer canthus, the whole being about the size of a grain of corn and elevated about two millimeters. This condition had existed for about six months, the growth having gradually increased to this size. The appearance is that of a gray-blue soft tissue, with numerous minute blood vessels irregularly distributed throughout the whole area. The tumor was so near the edge of the pupil that the patient had to slightly turn his head to the left when looking straight ahead.

The diagnosis made by Dr. P'Pool was epithelioma of the cornea, a diagnosis which was concurred in by Dr. E. Simonton, of Shreveport, La., and proven by a

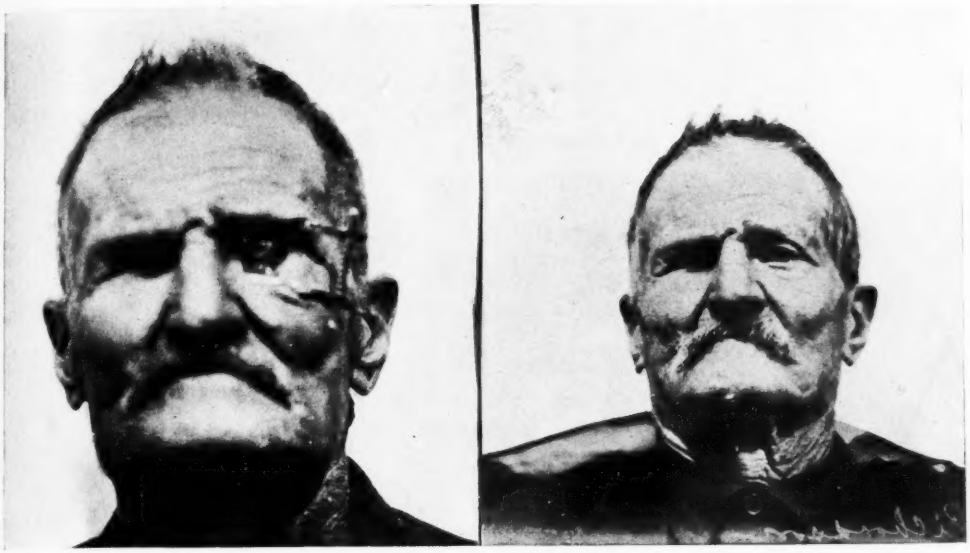


Fig. 2, Case II.

study of the tissue in the laboratory of Drs. Ellis and Butler.

The treatment in this case consisted in the use of two gentle doses of radium, 10 mg. hrs. being applied on October 8, 1923, using three 5 mg. needles applied directly to the surface of the growth. On October 24th, the condition was markedly improved and about 5 mg. hrs., using the same technic, was again applied. This produced a complete disappearance of all symptoms in the eye after the lapse of about three more weeks.

The two epitheliomas at the angles of the jaws yielded promptly to one full dose of X-rays.

This case is reported because of the comparative rarity of epithelioma of the cornea, the promptness with which it yielded to treatment, restoring the patient the use of the only eye which he had.

POLYPOSIS LOCALIZED IN THE TRANSVERSE COLON

REPORT OF A CASE

By THEODORE S. SWAN, M.D., Fellow in Medicine, The Mayo Foundation, ROCHESTER, MINNESOTA

A woman, aged forty-three years (A425272), registered at the Mayo Clinic May 10, 1923. She complained chiefly of diarrhea, of twelve years' duration. She had had from four to five watery brown stools daily, from breakfast to noon, as a rule, the stools coming usually with much gas and urgency. There was no tenesmus or griping, no blood, pus or mucus; occasionally there was slight involuntary soiling at night. After about six months her home physician gave her powders, and she had from three to four formed stools a day. At the end of a year the powders were stopped, and the diarrhea promptly recurred, but was not again controlled by the powders. Another physician was consulted who advised a low residue diet, without benefit. A third physician advised the same form of treatment, but the diarrhea became progressively worse; there were from six to ten watery stools, mostly in the morning. The patient became fatigued, although she lost only 10 pounds in weight. Her color remained good. Occasionally she would go to bed for five or six days; the number of stools then decreased, and sometimes were formed. The stools passed with a gush and much gas, but without froth. In 1920 the patient passed several stools of

"liquid bright red blood." This led her to consult a city specialist, who gave a negative proctoscopic report, but positive report of "ulcers of the large intestine," shown by the X-ray. Several stool examinations were

Fig. 1. Central filling defect in transverse colon. The upper and lower margins are not affected; this feature is characteristic of benign tumors generally.

negative. Silver nitrate enemas were given for three weeks, and the patient was well for three months, having two formed stools daily on full diet. Then the diarrhea recurred; but with powders, and rest in bed a few days at a time, she had more or less relief until September, 1922, when she again resorted to treatment, and was given kerosene enemas daily for one week, then less frequently and put on liquid diet until December, 1922, when she had two gushes of blood. The patient thought no benefit came from the kerosene. While on liquid diet she had had three or four stools daily and gained in weight and strength. In the last three weeks the diarrhea had become more severe, with lower abdominal distention and borborygmus.

On physical examination, the abdomen was found to be very tympanitic, 3 on a basis of 1 to 4. Laxity of the anal sphincter was noted. In a twelve-hour specimen of urine (350 c.c.) the specific gravity was 1.022, acid, albumin 1, pus 2, cells 45; a catheterized specimen was acid, albumin 1, pus 1, cells 5. The hemoglobin was 76 per cent; the erythrocytes numbered 5,070,000 and the leukocytes 9,000. The differential count showed: leukocytes 9,000, large mononuclears 3, transitionals 2, neutrophils 66.5, eosinophils 1, and basophils 0.5.

A test meal revealed acidity 34, with free hydrochloric acid 20. X-ray examination of the stomach revealed negative findings; of the colon, a lesion of the transverse colon (Fig. 1). Proctoscopic examination of 20 cm. of the rectum was negative. On three examinations of the stools the findings were negative. A clinical diagnosis of lesion of the transverse colon was made and exploration advised.

May 24, 1923, a high straight rectus incision was made and a polyp, 6 by 6 by 2 cm., was found near the middle of the transverse colon. The transverse colon was loosely attached and could be easily lifted from the abdominal cavity, and for this reason a first stage Mikulicz operation was performed, after the two limbs of the colon had been sutured together. In order to relieve the gas tension temporarily, an appendicostomy was performed through a stab wound, a catheter being passed through the appendix, after it had been drawn through the abdominal wall. Exploration of the stomach, duodenum and pelvis was negative. There seemed to be a mild cholecystitis, but no stones could be felt. Pathologic examination revealed papillary adenoma.

July 4, a second stage Mikulicz operation was performed. A loop of bowel, which contained the growth, attached apparently to the wall of the bowel, was cut with cautery. August 23, the two ends of bowel, which had resulted following the first and second stage Mikulicz operations, were freed from the abdominal wall and

closed. The appendicostomy, which had closed, was reopened, and a catheter introduced into the cecum. The patient recovered uneventfully, and was dismissed from observation August 24, 1924.

PHOTOGRAPHIC DARK-ROOM ILLUMINATION, AND FLUOROSCOPIC DARK-ROOM ILLUMINATION

By E. B. KNERR, M.D., Radiologist for Research Hospital, KANSAS CITY, MO.

Every photographer knows the use of ruby light for illumination of his dark-room. A great advance over the ruby light, however, has been attained in the substitution of green and yellow, combined by passing the light through screens of these colors.

The human eye is more responsive to green-tinted illumination than to any other color, doubtless because of the influence of the green tints of natural surroundings during the eons of its evolutionary development. The green of trees, grass and herbage in general has always been impressing its influence on the retina, whereas the red impression from natural sources is comparatively rare. Therefore, in a dark-room illuminated by green light all objects are more distinctly seen and the tones of a developing plate more acutely appreciated than is possible under any other illumination safe to the exposure of the sensitive plate or film.

That other old-time idea that for the safety of the sensitive plates the walls, shelving, etc., of the dark-room should be painted black is likewise fallacious. Instead of black the dark-room should be painted white or light gray. The white walls will reflect only such rays as fall upon them and under the proper green illumination only photographically safe green light will be reflected, and there will be no danger of fogging plates. With such a volume of green light reflected from the walls and furnishings of the dark-room the comfort, as well as the efficiency, of the operator's eyes is beyond compare to that experienced through ruby or any other illumination.

A similar great advantage may be attained in the fluoroscopic dark-room of the X-ray practitioner by a proper illumination of the room. The total darkness usually sought for in the X-ray fluoroscopic room is not necessary or even advisable. Much advantage may be secured to fluoroscopic observations by having the room faintly illuminated by a dull or dim olive-green light, in tint approaching as nearly as possible that particular tint which is optically complementary to the color given off by the actuated fluoroscopic screen. This particular tint may be determined accurately by proper spectroscopic study with suitable screens for color and other apparatus employed in investigations of optical physics. But also the desired color of illumination may be determined by any observer for himself by first determining the color optically complementary to his color impression of the actuated fluoroscopic screen. He may readily do this by diaphragming his fluoroscope to a square of about five inches to the side, and then steadily gazing on the screen in action for a full minute or two with the room darkened. Then continuing his gaze on the field of the screen let him cut off the current or close his eyes and in a few seconds he will see an afterglow of the dimensions of the screen while it was in action, but the color will be the exact complement of that given by the screen in action. The illumination of the room should be of the same tint as this complementary afterglow mental impression, faint but of sufficient intensity to distinguish objects about the room, and it should be continued during all fluoroscopic work.

THE ADVANTAGES THAT SUCH ILLUMINATION OF THE FLUOROSCOPIC ROOM HAVE FOR THE OPERATOR, CONSULTANTS AND THE PATIENT, AS WELL

The eyes of the operator and observers are accommodated much more quickly and acutely to the fluoroscopic light on the op-

tical principles of retinal fatigue and the accentuated brilliancy of complementary colors in juxtaposition. Under the diffused, faint illumination of the room, the retina is rested for the particular tint of the actuated fluoroscopic screen so that when the screen is in action the mental impression of its brilliancy is enhanced and the contrasts of its shadows deepened. Then if the eyes are diverted momentarily from the screen, or if the current is cut off, the impression of the general illumination tint of the room is enhanced, for the retina has been rested for that color. When again the screen is actuated its brilliancy in turn is augmented and the contrasts of the picture accentuated.

There is a great relief to the patient, as well, for he escapes all the nervousness attendant on manipulations in a totally darkened room, and the faint light of the properly illuminated room is agreeably reassuring to him.

The advantages to assistants, technicians and nurses will at once be appreciated, as, for example, in giving barium meals, rectal and sinus injections during fluoroscopic examinations.

The lamp furnishing the illumination desired should be so installed as not to cast direct rays into the faces of the observers or upon the glass surface of the fluoroscopic screen, causing interfering reflections. The principles of indirect illumination should be followed.

The writer has been using this method of fluoroscopic room illumination for several years and feels that its advantages should be more generally appreciated.

CELLULAR FIBROMA ERODING THE SPINE

REPORT OF A CASE

By CHARLES G. SUTHERLAND, M.B. (Tor.), Associate in Radiology, Mayo Clinic, ROCHESTER, MINNESOTA

Case A142990, a girl, aged twenty years, was admitted to the Clinic October 8, 1915, with deformity of the dorsal lumbar spine, paralysis of the lower limbs, and partial incontinence of the urine and feces. Until four and a half years before, she had been a healthy, athletic school girl. She

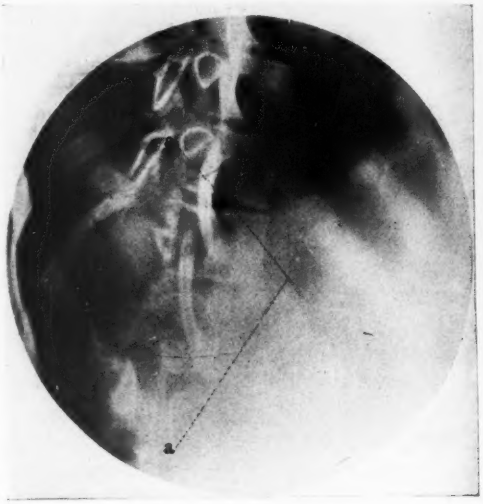


Fig. 1 (A142990). Destruction of the laminæ and processes of the twelfth dorsal, first and second lumbar vertebræ.

then had begun to have sudden attacks of falling, without pain or premonitory symptoms. She could get up immediately and walk normally. Without apparent reason, she fell while playing basketball. Three months later she had difficulty in going upstairs, more marked in the right leg. Six months later definite paralysis of the right foot muscles developed, followed by a gradually ascending sensory and motor paralysis of the right, and later, of the left leg. At the end of three years there was almost complete paralysis of the hips. Urinary and fecal incontinence developed. Two years from the onset, a small mass, not tender on pressure, was noticed on the right of the twelfth dorsal vertebra; this had progressively increased in size. A roentgenogram made one week before examination revealed a lesion of the twelfth dorsal vertebra on the right side.

The patient was well nourished; there had been no loss of weight, and the physical findings coincided in general with the foregoing history. The roentgenogram disclosed destruction in the twelfth dorsal and

Fig. 2 (A142990). On the left the tumor removed from the muscles of the back; on the right the tumor removed from the spine at the second operation.

first and second lumbar vertebræ. A diagnosis was made of compression myelitis from a lesion of the spine, either tuberculous or sarcomatous.

At operation, October 18, a tumor, 5 cm. in diameter, was found projecting through the muscle; this was completely removed. Macroscopically the tumor suggested sarcoma, but microscopically it proved to be fibroma. After corroboration of the diagnosis by fixed sections, a second operation was performed October 27, and a large fibroma was exposed, which had eroded the arches of the eleventh and twelfth dorsal vertebræ. The tumor was outside the dura, completely compressing the cord. It was irregular in shape, and extended from the ninth dorsal vertebra to the first lumbar, more to the right side than to the left, into the deep muscles of the back and over the edges of the ribs on the right, where it was adherent to the pleura. In enucleating the tumor the pleural cavity was accidentally opened and a definitely encapsulated portion of the tumor entered the pleural cavity, but this was removed without incident or sequela. In September, 1916, there had been no definite change in the condition as a result of the operation. In May, 1923, her physician wrote that she was still paraplegic, with level symptoms extending to about the first lumbar cord segment.

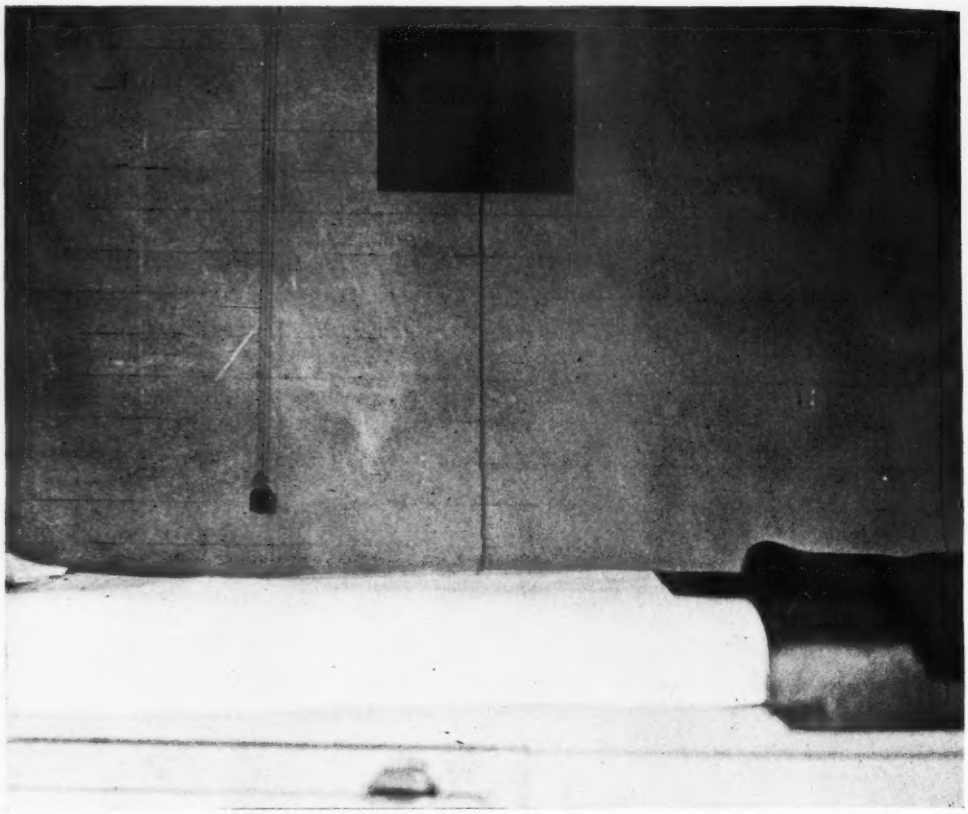
ANOTHER METHOD OF PREVENTING THE OMISSION OF FILTERS

Submitted by R. W. GIBBES, M.D., and F. D. RODGERS, M.D., COLUMBIA, S. C.

Dr. George E. Pfahler has presented two rather unique and practical ideas to prevent the omission of filters: one to be used where treatment is applied from above and the other for the couch type of equipment. We are publishing herewith a photograph of a method that we have found practicable and safe for the couch type.

Our filters are 11 by 11 inches. We have secured a heavy piece of cardboard of the same dimensions, soldered a short loop of wire to the filter, and fastened one end of a piece of cord to the cardboard and the other to the filter. We have printed on the cardboard in rather large letters the thickness of the filter. There is one piece of cardboard permanently attached to each filter, and when a change of filter is made the piece of cardboard attached to that particular filter is hung on the wall in plain view, so that at all times one is able to see that there is a filter in place, and its thickness. (See illustration on page 60.)

We believe this method has the following advantages: (1) There is no electrical device to get out of order and so fail to give warning; (2) It requires manual manipulation to make the change; (3) One can know the thickness of the filter without disturbing the patient; (4) No card on the wall means no filter in place; (5) Simplicity and inexpensiveness.



A device to prevent the omission of filters (see page 59).

CORRESPONDENCE [1]

Excision of a V-Shaped Piece of the Lower Lip Versus Roentgen-Ray or Radium Treatment

By JOSEPH COLT BLOODGOOD, Baltimore, Md.

To the Editor—This morning (Nov. 3, 1923) a patient presented himself with a mass the size of an egg in the submental area and apparently somewhat fixed to the lower jaw. In March, seven months ago, a small ulcer on the lower lip was subjected to radium treatment and has healed, leaving a slight, umbilicated scar. The lesion, whatever its nature, had been present three months. It occupied the mucocutaneous border of the middle third of the left lower lip. It had apparently begun as a smoker's burn in a patient with bad teeth.

These cases are increasing in number. That is, the lesion on the lip heals, or apparently heals, after the application of roentgen rays or radium, and then, a few months or years later, glands appear in the neck, which, when removed, prove to be metastatic carcinoma.

I would appreciate an opportunity to present to the larger audience of the readers of *The Journal* the following facts:

Some years ago I made one report on the operative treatment and results of cancer of the lip, and there is in preparation a second report on a larger number of cases. The conclusions of the first report are confirmed by the restudy of both old and new

[1] Reprinted from *Jour. A. M. A.*, Vol. LXXXI, Nov. 24, 1923, p. 1807.

material, and the ultimate results up to date.

If the lesion on the lip can be excised with a V-shaped piece and the wound closed without a plastic operation, there has never been a local recurrence, irrespective of the pathologic condition, whether the lesion was benign or malignant. This operation can be done under procain within one-half hour, and the patient should not lose more than a few hours from work.

The cost of such a minor operation in material and in time of patient and operator is small as compared with that of any other treatment, and it is my opinion that the results are the best.

The piece excised from the lower lip is subjected to microscopic study, and if the sections show cancer, the glands of the neck are removed (this can also be done under procain). When these glands show no evidence of metastasis, the percentage of cures has been 100. When the glands have shown metastasis, the percentage of cures in the first report was 50, and in the second report will be somewhat larger.

Now that the community is educated to seek advice early, the moment the lesion is observed on the lower lip, I am able to divide the cases observed and reported by me into the following classes:

1. The lesion on the mucocutaneous border of the lower lip is small, of short duration—a few days up to two weeks; it is of the type of a burn, a fever blister, a vesicle, keratosis or a wart. The patient smokes or chews; the teeth may be ragged and dirty. The majority of these lesions heal by removal of the causes—tobacco and ragged, dirty teeth—and instructing the patient to keep the teeth clean and the lip lesion covered with petrolatum.

2. The lesion is of longer duration, but still distinctly benign—leukoplakia, or the chronic chapped lips of the smoker. Such lesions disappear when tobacco in every form is removed.

3. The lesion of the first group does not disappear under treatment, or, when seen, is of longer duration. In this group one cannot distinguish between the benign and the malignant, clinically.

4. The lesion is distinctly benign—a wart.

5. The lesion is distinctly cancer.

Groups 3, 4 and 5 should be subjected to immediate local excision under procain, and the operation on the glands of the neck performed, if the microscope pictures carcinoma in the primary lesion.

If, instead of operation, these patients are subjected to radium, roentgen rays, caustic paste, fulguration, cautery—all without microscopic study—the lesion in the first group will be permanently cured, but the treatment deserves no more credit than the treatment by the removal of the cause and cleanliness.

In Group 2, no treatment is of any value, unless the cause (tobacco) is removed, and if this is done any other treatment is unnecessary.

In Group 3, any other treatment that does not permit a microscopic study will lead to the false conclusion, in many of the cases, that the treatment has cured a local cancer; and if the local lesion is malignant, just as in Group 5, the removal by operation, or the destruction or healing by any other treatment, is but a minor part of the treatment. It is essential to ascertain whether the local lesion is cancer, and if it is, to remove completely the glands in the submaxillary and submental areas. Today there is every evidence that complete removal of the glands of the neck offers more than any other known treatment. There is apparently no objection to irradiate, either with roentgen rays or with radium, the lymphatic area before and after the thorough removal of the glands; but there seems no question that the removal of the glands is the essential feature. In those cases in which the microscope fails to show metastasis, post-operative irradiation is unnecessary.

I am willing to submit the accumulated evidence in the Surgical Pathological Laboratory of the Johns Hopkins Hospital

to any investigating committee for comparison with roentgen ray, radium or any other type of treatment. This second paper will soon be published. In view, however, of the growing tendency of members of the medical profession, not surgeons, to refer their patients with early lesions of the lower lip for roentgen-ray and radium treatment, it was my opinion that this warning, based on thirty years' experience with more than 500 cases, should be made, if possible, with the largest publicity.

At the present time more than 60 per cent of the lesions that I have excised from the lower lip are microscopically benign, and of the remaining 40 per cent, in more than 75 per cent the glands, when removed, show no evidence of metastasis.

Effects of X-rays on tissues.—The exact mode of action of X-rays on cells is not definitely known; it seems to be mainly on the nucleus, particularly on the chromatin material and especially during division of the cell. Its action is not specific, but seems to inhibit growth so that the cell dies from exhaustion or old age. It is assumed further that undifferentiated and young cells are more easily killed. A peculiar feature of the X-ray effect is the latent period, which varies with different types of cells, being short in the case of leukocytes and longer in epithelial cells of the skin. The reason for this latent period has not been satisfactorily explained.

The basis of X-ray therapy is the assumption (not accepted by everyone) that tumor tissue is more susceptible than normal tissue. Loeb explains this vulnerability by the rapidity of growth, the generally unfavorable environment and the lack of sufficient paraplasmic substance. The question of selective action has become of greater importance with high voltage X-ray applied to deep-seated tumors, because of the normal tissue traversed by the ray and the circulating blood through the area treated, so that the effect of X-rays on different tissues becomes a matter of great importance.

The reaction of tumor tissue to X-ray and radium is quite specific, but varies with the dosage, the nature of the tumor and the susceptibility of the individual. After radiation of squamous cell carcinoma of the cervix, hyperemia is the first change; edema is noted in the stroma on the third day, followed by exudation of lymphocytes and leukocytes. During the second week nuclear changes in the cells occur, the nuclei becoming swollen, homogeneous and hyperchromatic. The cell bodies are loosened and may fuse into giant cells; tumor alveoli begin to disintegrate; there is abundant leukocytic infiltration and mitosis no longer occurs. During the third week after a single treatment, tumor cells become necrotic and liquefied, cell clusters are broken up or compressed by lymphocytes. After four or five weeks, pycnotic nuclear fragments and agglutinated masses of chromatin may be all that is left of the tumor masses, and capillaries and fibroblasts proliferate, forming granulation tissue to replace the tumor tissue. If the dose is exactly adjusted, the healing occurs without scarring. If dosage is too great, vessels are destroyed and a dense hyaline scar results, which prevents the reaction of the normal tissue.

In X-ray therapy two cellular reactions occur, one a destructive one on the tumor cells and the other a stimulative one on the natural body defenses. For optimum effect, the dose needs to be nicely adjusted. There is no such thing as a "fixed carcinoma dose." The roentgenologist has three biological variants and one stable factor. He is sure only of the X-ray dosage, and has the individual patient, the location of the tumor and the nature of the tumor as variants. Radiological judgment, therefore, is more complex and difficult than surgical judgment and demands more fundamental knowledge of physics, chemistry, biology and pathology.

W. W. Watkins, M.D.

Cellular Reactions Following X-ray and Radium Therapy. H. R. Wahl. Mo. St. Med. Assn. Jour., June, 1924, p. 173.

EDITORIAL

WILHELM CONRAD ROENTGEN[1]

HIS LIFE AND WORK

By I. SETH HIRSCH, M.D., NEW YORK CITY

WHEN, in compliance with the request of our President, I consented to speak on the life of Roentgen, it seemed to me that more vital and interesting than merely to review the events of his life would be to study his character and personality and the bearings these had on his scientific labors, and to consider his career from the standpoint of the light it throws on the spirit of the age and the lesson it carries to even the humblest worker.

It is as difficult, says Strachey, to write a good life as to live one, but so striking is the personality of Roentgen, so inspiring his life's story, that the task invites performance. It is always of interest to study a great man with a purpose of seeking out the impelling motives of his life, the springs of his actions, his aims and endeavors; it is instructive to analyze the events which guided his life into those channels of human activity wherein he achieved fame, to fathom by what odd chance, what shifts and struggles, what combination of circumstances and character played a part in his arrival at distinction.

Roentgen grew up in the very seedtime of progress, coming to the full bloom of maturity with the first onrush of modern science and living long enough to witness its tremendous victories and the complete revolution of scientific thought. And what a revolution it has been! How striking the contrast between the self-satisfied complacency of the physical world before Roentgen's discovery, regretting there were no more worlds to conquer, and the feverish activity in the endless paths, now but dimly envisioned, leading to regions containing truths tremendous in their import to humanity.

Wilhelm Conrad Roentgen was born in Lennep in the Rhineland on the 27th of March, 1845, and died on the 10th of February, 1923.

In his famous essay, "Concerning Human Understanding," Locke tells us that the child's mind is essentially a blank tablet upon which nothing is written, and that all knowledge rests on experience. Let us, therefore, pause for a moment to consider the childhood of the character we are studying. What were the childhood experiences, influences and relationships, which definitely moulded his character?

Since parental images are the models engraved on the growing mind which serve as standards and determinants in later life and influence adjustments in the workaday world, it is interesting to note that he was an only child of a German father and Dutch mother. It has been pointed out that, properly brought up, the only child possesses attributes which tend to leadership, and some of the greatest leaders in all walks of life were only children. Roentgen's childhood was a very happy one and was spent in Utrecht, Holland, the birthplace of his mother. His father, Frederich Conrad, was a farmer, a man of the soil, simple, reserved, taciturn and religious. From him he inherited the qualities of industry, of patience, of directness

[1]Read before the Radiological Society of North America, at Rochester, Minnesota, in December, 1923.
For many of the facts in this address the author is indebted to articles by Koch, Friedrich and Sommerfeld and to personal communications from friends.

of action and perseverance in life's efforts and strivings. From his mother came those great qualities of imagination, love of truth, simplicity and modesty.

The child, thus, grew up in an atmosphere of piety, thrift and orderliness, into a sturdy, modest and reticent boy. After a few years of primary schooling it was planned that he should follow the agricultural occupation of his father and to this end he entered the agricultural school at Apeldoorn, Holland. There are glimpses of him at this time as a wide-awake boy, of no extraordinary ability, not very studious, but deeply interested in Nature. He apparently entered keenly into the rivalries incidental to the physical activities of childhood, and already then evidenced certain qualities of distinction among his fellows. About this time an incident occurred which not only gives proof of a high standard of honorable conduct, but was instrumental in eventually deviating his career into those paths of endeavor where he achieved greatness. Accused of some harmless schoolboy prank, while in the fifth year at school, he frankly admitted his part in it, but his sense of honor would not permit him to reveal the names of his companions in mischief, and for this refusal he was dismissed. This was a great blow, because it seemed to bar the way planned for him. His sorrow was tempered only by the faith his mother had in him and by the fact that she understood and appreciated the dignity and courage of his attitude. He did not complain, but bore it stolidly, though the possibility of a higher schooling now seemed remote. Later in life, when confronted by slander and calumny, he bore it with the same fortitude and silence, strong in the knowledge that his actions were honorable and that the truth and right were his.

He attempted to pass the promotion examinations of the first grade of secondary school, which would have permitted him to matriculate without any further examinations in a German university, but failed.

Little did he dream that these apparently trivial incidents, which to him seemed so calamitous, were really a blessing in disguise. They permitted a development along the lines by which his innate capabilities were unfolded. They saved him from the educational system, which seeks to repress all tendencies to diversity of mental development and to conform all heads to one mould. Nature loves diversity. The educational machine aims at repressing it. Did not Duclaux, the successor of Pasteur and his biographer, point out that those who show originality and achieve distinction are recruited chiefly from the ranks of those who have escaped the sterilizing influence of the early years of standardized education?

Thus his boyhood passed, on the whole given more to contemplation than action. Less prosperous, it is true, in fortune than he might have been, but doubly fortunate in a solitude which permitted him to read and to dream. He lived in a realm of the imagination and became thus early,—as he was to continue all through life,—something of the idealist, constructing the world for himself in a great measure from within by the exercise of the meditative power.

Because the Polytechnical Institute in Zurich accepted students without matriculation examinations, Roentgen entered the school. Here he was not the assiduous student, glued to his task; no hustler was this young man who loved the stones, the woods and flowers; no bookworm, absorbed in his daily task, but a dreamer, who hated the grind of the routine and forsook it for the sky-towering mountains of the Engadine, in whose shadow the school stood. The clouds resting on the icy peaks, the shifting panorama of lights and shadows, the glorious vistas of these mountains fascinated him, even to his old age,—yes, almost to his dying day he dreamed of them. Every year he came to them in the Park Hotel in Pontresina. They will tell you there of the days he would spend in the vast silences of the glaciers, fascinated and inspired. In the great solitude—far away and above the insistent trivialities of life—

would come to him that clearness of vision, that confidence in himself and strength of purpose so necessary to baffling research.

But there was one personality at the university who, for him, was as a mountain peak—Clausius, who at this time was teaching physics, and the young student listened with rapt attention to this teacher, renowned for his researches in the field of theoretical physics. It was thus his good fortune to hear from its original propounder, of the mechanical theory of heat production, of the kinetic constitution of gases, of the characteristics of molecular movement in gases. Under the inspiration of this teacher, the imagination of the Nature-loving student was stimulated and he saw in the vistas of thought opening to him, a further unfolding of the beauties and mysteries of Nature, which from the first sentient moments were the wonder and concern of a mind and spirit sensitized by this priceless inheritance.

Though never properly entered in the School of Experimental Physics, nevertheless drawn by an irresistible interest he became a voluntary student, zealously attending the lectures, showing great preference for and interest in the exact experimental work of physical research, particularly in questions of a technical nature. In this field he manifested an extraordinary aptitude, especially for work requiring exactness and detail. This interest, industry and ability won him, immediately after graduation, an assistantship to Kundt, whose favorite pupil he was and with whom he was associated for many years. It was for the work done with Kundt that he received from the University of Zurich his degree of Doctor of Philosophy. Roentgen ever held Kundt in the highest admiration as his teacher and his guide. To him he owed much of his experimental skill and the thoroughness and exactness which characterized all his investigations.

When Kundt was called to Würzburg he took young Roentgen with him. In Würzburg he met the woman he married, who during a long life was his devoted companion, aiding and comforting him through his career.

The difficulty in his high school period, to which reference has been made, seems to have placed an insurmountable obstacle to progress in his academic life. In spite of strenuous efforts on the part of the teacher, it seemed impossible to obtain a place for Roentgen on the staff of the University. Bureaucratic German officialdom would not recognize this young student, whose primary education seemed incomplete and whose social connections were unimportant. Luckily for him, Kundt was called to the professorship of the newly founded Strassburg University. There the traditions were not so strict as in Würzburg, and in two years he received the Dozentship in Physics. From that time on his progress was rapid. At the age of thirty, he was appointed Professor of Mathematics and Physics in the Academy at Hohenheim, but left the following year, at Kundt's request, to return to Strassburg, where he assumed the position of Associate Professor of Theoretical Physics.

Three years later, at the age of thirty-four, he was called to Giessen as full Professor of Experimental Physics. There he remained almost ten years, happy, busy, occupied chiefly with his pupils, but nevertheless devoting much energy to experimental work. He lived in the serene peace of the laboratory and the library, studying, investigating, and laying firmly the foundation of his future work. Here he made numerous lasting friendships and always counted these days as among the happiest of his life. In 1888 he accepted the call to the University of Würzburg. His rapid advance in academic standing thus plainly testifies to his great ability as an investigator and his excellence as a teacher and organizer.

It was as Director of the Physical Institute in the Würzburg University, at the age of fifty, that he discovered the X-rays.

(To be Continued)

SCIENCE HAS ITS HEROES

An Appreciation of Professor Bergonie, Bordeaux, France

By Warren L. Babcock, M.D., Director, The Grace Hospital, Detroit, Michigan

The death of Professor J. Bergonié, of Bordeaux, brings to the attention of pioneer radiographers and roentgenologists, the experimental work and personal characteristics of the premier French pioneer in this work. Professor Bergonié, as early as the beginning of the century, realized that before the effects of roentgen rays on pathological tissue could be measured and appreciated, it would be necessary to know positively the effects on living cell structure. For many years he carried on experimental work on the effects of roentgen rays on the living cells in both humans and animals. His pioneer work in this line was instantly felt in professional circles on the Continent and reflected in this country.

This brief appreciation is not the place for details of his experimental work. Suffice to say that his death can be directly traced to his courageous and sacrificing study. Before he fully appreciated the effects of the rays on normal living structures, he was badly burned about the hands and right arm. Several years ago these burns necessitated the amputation of several fingers, and in 1922, his right arm was amputated at the shoulder. At this time he was nearly seventy years of age, but he rallied from his operation and was soon back to work. His industry and will were indomitable and he carried on.

Directly after the war he became deeply interested in the subject of cancer control and was one of the first workers in France to suggest the regional control of this disease. He ably assisted the French Minister of Hygiene, Dr. Paul Strauss, in the organization of the provinces of France for the regional control of cancer. He was made Director of the region of Bordeaux and the Southwest. His later years have been devoted largely to this work, in addition to his teaching and private practice.

"In the university cities, these centers take advantage of the technical skill and the scientific knowledge of professors in the medical schools. The organization of these regional centers comprises: a consultation service for the detection of cancer, for its early diagnosis, including a pathological examination, a surgical service, a roentgenographic service for deep roentgenotherapy, and a radium therapeutic service. The administration of the hospitals or the *faculté de médecine* furnishes the quarters and the auxiliary personnel. The heavy expenditures for the apparatus required for deep roentgenotherapy and the high cost of radium supplies are covered by various appropriations and gifts—from the central government, the departments, the cities, private individuals, and other sources. The annual budgets of these regional centers are provided for in the same manner. Patients who are receiving free medical treatment in the departments are sent, with their travelling expenses paid, to the regional consultation center. Here they are examined, treated, and, if necessary, are transferred to a hospital and the expenses charged to the chapter of the department concerned."

It is to be remembered that during his early experimental work on the effects of roentgen rays, and his public and experimental work in cancer control, Dr. Bergonié conducted a large clinic in Bordeaux, was the Director of the Department of Roentgenology of the University of Bordeaux Medical School, and maintained a very large hospital and private practice. Few workers in any specialty have been able to devote more hours and energy to

their work than Dr. Bergonié and, like most savants, he was made happiest thereby.

It was the great privilege of the writer to be intimately acquainted with Dr. Bergonié during the past six years and in frequent association with him for over a year during the war. Although he was well over sixty years of age at the time, he played a prominent part in the World War and was in the service from an early date, attaining the rank of Colonel. During most of the war he was the Commanding Officer of French Supplementary Hospital No. 4, one of the largest military hospitals in Bordeaux.

He must needs be original, even in war service, and was the instrument for the introduction of many reforms in French military hospitals, and especially in developing an entirely new departure in the treatment of convalescent wounded. This was known as the "French Cures Agricoles." These were scheduled stations in the Girondin vineyard country where groups of convalescent ambulatory wounded were distributed, housed in French homes or chateaux, and utilized in light work in the vineyards. The country life, freedom from hospital environment, and personal freedom and experience greatly contributed to the repair of many forms of wounds and wound sequelæ, especially as Prof. Bergonié utilized physiotherapy and local exercise in conjunction. His success in this endeavor so impressed the American military authorities that in 1918 they made arrangements, with his influence, to have American convalescent wounded sent into the vineyards from American Base Hospital No. 6, near Bordeaux. The work initiated in this direction by Prof. Bergonié was used elsewhere in France by other divisions of the military service, and he can be credited with its initiation.

In social intimacy he was one of the most charming of men, as will be attested by a considerable group of American officers of all lines of the service, who partook of his hospitality at La Floquette. His "week-ends" for American officers at his summer home will never be forgotten by those who were privileged to participate. In this he was ably seconded by his charming and helpful wife, who survives him. The following characteristic but not overdrawn editorial by Arthur Brisbane may well be quoted here:

"Everybody knows that in courage the French are excelled by no race on earth. The Gauls, telling Alexander that they feared nothing except that the heavens might fall on them; proud Vercingetorix, dragged behind Caesar's chariot; the noble d'Assas, 'dead on the field of honor'; Crillon and Du'Guesclin, their bodies covered with scars—in front; the Frenchman who held on to the enemy's boat with his elbows, after both his hands had been cut off—they all live in glory.

"Science produces a new and greater French hero, Dr. Bergonié, of Bordeaux, who has just died, killed by his constant use of radium in his warfare against cancer.

"Weakened by radium bombardment, to which they were constantly subjected, his tissues were attacked by the cancer that he sought to conquer. His right arm was cut off, and then three fingers of his left hand. He continued at his work to the day of his death, experimenting with and lecturing on the effects of radium on the gangrene that attacked one of his remaining fingers.

. . . . .

"That's real courage, quiet heroism without the excitement of the battlefield, or crowds applauding, fighting the battle of science against cancer, enemy of the entire race.

"How many will remember the name of Dr. Bergonié next week? Not one in a million of those who will distinctly remember the name of John L. Sullivan."

The Radiological Review, a bi-monthly journal devoted to the progress of X-ray and radium as it relates to the practicing physician and dentist, is a new journal published by the Radiological Review Publishing Co., at Quincy, Illinois.

ADVICE AND WARNING REGARDING PROFESSIONAL LIABILITY INSURANCE

At the Meeting of Special Committee on Laboratories, Medical Society of the County of New York, October 21, 1924

Those present were Mr. George W. Whiteside, Counsel for the Medical Society of the State of New York; Mr. H. V. Wanvig and Dr. Weston of the Aetna Insurance Company; Dr. Byron C. Darling, Chairman; Dr. H. M. Imboden, New York City; Dr. Charles Eastmond, Brooklyn. Besides these there were present as invited guests Dr. M. J. Sittenfield of New York and Dr. Henry Schmitz of Chicago.

The subject for consideration was the state of professional liability insurance for physicians using the X-ray for diagnosis and therapy, and radium for therapy.

Mr. Whiteside explained how the insurance company had had about fourteen unsettled X-ray suits, which was estimated to be about fourteen times the usual percentage of suits for all practitioners. The insurance company had therefore required a rider for this work, with an increased rate, to be continued for two or three years in order to get experience statistics, and the results of the suits now pending. The increased premium will call the attention of the general profession to the increased liability and will serve as a warning. It was generally agreed that radiologists should give this matter careful consideration in order to cut down on their losses; that the Radiological Society of North America and the American Roentgen Ray Society should call the attention of the general medical profession in some way to the situation, and to the dangers inherent in the high tension current and in the use of the X-ray for picture work and fluoroscopic work, and particularly in the matter of therapy, both X-ray and radium.

Some of the factors causing the suits are:

1. The disappointment of the patient; the psychological reaction in the face of a bad end-result. Too much may have been promised, with little emphasis on the possible unsatisfactory outcome.

2. Computation of dose, filter, distance, time, etc., must be correct and a matter of accurate record, and should be signed by the full name of the technician.

3. The delegation of treatment to technicians brings in many new questions of law. Technicians should be competent and experienced, and each treatment should be under medical supervision to check up the filters, time, etc. Each treatment card, having been signed by the technician in charge, should be initialed or signed by the physician so that he knows he has seen that particular patient and that the patient has seen him.

4. Previous history in X-ray and radium treatment cases should be a matter of careful record. This should include a careful and complete record of other treatments, with written statement of the amount, date and character from the former physicians, and also previous medication which would influence the reaction to the radio-therapy.

5. The patient should sign the history, which will cut down about 80 per cent of the loss according to Dr. Weston of the Aetna Insurance Company, as a signed history becomes a matter of evidence, and knowledge of the existence of this discourages attorneys from taking such suits for the plaintiff.

6. The patient may properly be asked to sign a waiver to the effect that he is taking his own risk and waiving any suit. This, however, does not relieve the practitioner from liability for proven ignorance or neglect.

7. In hospital work particularly, absence of adequate data, history of dosage, name of the technician giving the treatment, and general informality of records make a proper and satisfactory defense difficult.

8. Charity cases are no exception and

carry the same liability, whether in private offices or hospitals.

9. Cosmetic damage is an additional risk and facial beauty of unmarried females, actresses, etc., is an important item.

All this only goes to emphasize the care and foresight necessary, and that all technicians should be carefully chosen and trained; it would be an additional help in time of trouble to have them registered with the American Registry of Radiological Technicians. The recommendations of the Safety Committee of the American Roentgen Ray Society are of the greatest importance in this connection.

Another important factor is that of the attitude of the manufacturers. During wartime, like other businesses, they reached a quantity production basis, and the slogan of some has been to put some small or large X-ray outfit in every physician's and dentist's office. It is for the medical and dental profession to digest this whole proposition carefully both from a professional and economic point of view, for if a reaction is to set in until only the specialist, who is aware of the dangers and technicalities of the work, who has trained not only himself, but who has a trained staff, is delegated by common consent of the medical profession to do this work, the sooner the manufacturers properly estimate the demand and the true state of affairs, the better off they will be, not to speak of the public and ourselves.

Standardization of apparatus: The designs are constantly changing and shifting.

The manufacturer should refuse to equip any unsupervised technician and should caution the inexperienced physician who contemplates such installation, rather than use high-pressure salesmanship. Some of the best known are the worst offenders.

Respectfully submitted,

BYRON C. DARLING, M.D.,
Chairman.

THE TENTH ANNUAL MEETING

The Radiological Society of North America held its tenth annual meeting in Kansas City during the week of December 8-12, 1924. This meeting was opened with an executive session Monday afternoon. The annual counselors' meeting convened in the evening, following the regular counselors' dinner. The reports from the committees and the counselors indicated that the substantial progress which has characterized the growth of this Society in the past has continued throughout this year. The reports from the Membership Committee and the counselors on new members show that the number of applications accepted far exceeds the number of names to be withdrawn from the roster for the following year, and the indications are that the total membership has reached well beyond the one thousand mark. There is no better argument for the importance of Radiology in medical practice than the size and quality of this organization.

President Stevens emphasized on several occasions his gratitude for the activity, promptness and thoroughness manifested by the various standing and appointed committees in their work during the year.

The Editor of RADIOLOGY was commended especially for his success in the management and editing of the official journal. The counselors voiced their approval freely in the work of the Editor and his associates and concurred in every recommendation provided in the Editor's report.

The scientific program was unique, in that seven very important clinical conferences were provided.

The first clinical conference was on "Carcinoma of the Breast: A Consideration of the Pathological, Surgical and Radiological Aspects." This conference was conducted by Dr. Burton J. Lee, Professor of Clinical Surgery, Cornell University, New York City. Other contributors to this conference were Dr. Harry Roswell Wahl, who spoke of the effects of X-ray therapy on tissues. Dr. M. B. Clopton, St. Louis, presented the

difficulties in the diagnosis of carcinoma of the breast from the surgeon's standpoint. The results obtained in the surgical treatment of carcinoma of the breast were aptly discussed by Dr. Jabez N. Jackson, Kansas City, Mo. Dr. John F. McCullough, of Pittsburgh, presented the radiological aspect of this conference in a paper on the results of radiological treatment of cancer of the breast. This conference developed a great amount of interest, and discussions by Drs. Henry Schmitz, Francis Carter Wood, A. W. Crane, Henry J. Ullmann, W. L. Ross and A. U. Desjardins added greatly to its value.

The second clinical conference on Bone Tumors was conducted by Dr. Henry W. Meyerding, Assistant Professor of Orthopedic Surgery, University of Minnesota, Mayo Clinic. Contributors to this conference were Dr. Willis C. Campbell, of Memphis, Tenn., who spoke on Bone Syphilis, and Dr. William C. MacCarty, Professor of Pathology, University of Minnesota, Mayo Clinic, who presented Pathological Types of Bone Tumors. Dr. Meyerding in conducting the conference spoke on Multiple Myeloma. This conference was discussed by Drs. L. T. LeWald, A. W. Crane, Max Kahn, L. R. Sante and W. H. Stewart.

The third clinical conference was conducted by Dr. W. W. Wasson, of Denver, Colorado, on the subject of Tuberculosis of the Lungs. "The Key Points in Lung Structure" was the subject of a paper by Dr. William Snow Miller, Professor of Anatomy, University of Wisconsin, Madison. Many years of research and teaching have eminently qualified Dr. Miller, and his contribution to this conference was received with unusual interest. "The Pathology of Tuberculosis in the Human" was the subject of a paper by Dr. Henry Kennon Dunham, Professor of Medicine, University of Cincinnati. Owing to illness in his family, Dr. Dunham was unable to be present and his paper was read by title. (The full contents of this paper will be published in RADIOLOGY in the near future and the members will have the opportunity to read the proceedings of the entire conference.) Dr. James J. Waring, Denver, Colorado, presented "The Relationship of the Radiological Diagnosis of Tuberculosis of the Lungs to the Clinical Diagnosis." "A Pathognomonic Radiographic Finding in Early Pulmonary Tuberculosis" was reported in a joint paper by Dr. Isador S. Trostler and Dr. Robert H. Hayes, of Chicago.

The fourth clinical conference was conducted by Dr. LeRoy Sante, Associate Professor of Radiology, St. Louis University School of Medicine, St. Louis, Missouri, on the subject of "Non-tubercular Diseases of the Lungs." A joint paper was presented by Drs. W. W. Watkins and Harlan P. Mills, of Phoenix, Arizona, on "The X-ray Evidence of Secondary Infection in Pulmonary Tuberculosis."

Dr. LeRoy Sante contributed a paper to this conference in which he spoke on "Acute Consolidations of the Lung: Their Recognition and Differential Diagnosis." Dr. William H. Stewart, of New York, presented a very comprehensive paper on "Pleural Effusions, General and Local: Their Detection and Differentiation from Lung Abscess." "Newgrowths of the Lung, Primary and Secondary: Their Classifications, Characteristics and Differential Diagnosis," was the subject of a paper by Dr. L. T. LeWald, of New York. A joint paper by Drs. Max Kahn and Martin F. Sloan, of Baltimore, Maryland, on the "X-ray and Clinical Study of Some Pulmonary Lesions," closed the conference.

The fifth clinical conference on the subject of "Teeth as Foci of Infection" was conducted by Dr. Boyd S. Gardner, Mayo Clinic, Rochester, Minnesota. "The X-ray Diagnosis," by Dr. Fred Molt, of Chicago; "The Bacteriological Aspect," by Dr. R. L. Haden, of Kansas City; "The Medical Aspect," by Dr. W. W. Duke, of Kansas City, and Dr. Gardner contributed "The Surgical Aspect."

The sixth clinical conference was conducted by Dr. E. L. Jenkinson, of Chicago, on the subject of Thyrotoxicosis. The subject was discussed from the medical

standpoint by Dr. John L. Tierney, of St. Louis, Missouri. Dr. E. P. Richardson, of Boston, Massachusetts, presented a paper on this subject from the surgical aspect. From the radiological standpoint papers were contributed by Dr. A. C. Christie, of Washington; Dr. Jenkinson, of Chicago, and Dr. R. G. Allison, of Minneapolis. "Thyrotoxicosis and Its Treatment with Radium" was to have been presented in a paper by Dr. Roland E. Loucks, of Detroit, Michigan, but owing to illness Dr. Loucks could not be present and his paper was read by title.

The seventh clinical conference was conducted by Dr. Byrl R. Kirklin, of Muncie, Indiana, on the subject of the gall bladder. Dr. Robert A. Arens, of Chicago, presented a paper entitled "A Clinical Radiological Study of the Gall Bladder." "The Radiological Diagnosis of Cholecystic Disease" was presented by Dr. Russell D. Carman, of Rochester, Minnesota. Dr. B. H. Nichols, of Cleveland, presented a paper on "The Differential Diagnosis of Gallstones and Kidney Stones." A paper by Dr. C. D. Enfield was read by title owing to the absence of the author. These contributions were discussed by Drs. Sherwood Moore, B. C. Darling, M. N. Garhart, H. J. Ullmann, W. G. McDeed, C. W. Geyer, and Wesley H. Wallace.

In addition to the clinical conferences the program was divided by subjects: For example, the conference on Physics and X-ray Therapy; the conference on Light Therapy; the conference on Radiological Education. The joint meeting with the Jackson County Medical Society, as well as papers on subjects not listed with any of the conferences, contributed a feature to program construction which proved to be very satisfactory. Because of this arrangement the members were able to visit the exhibits and enjoy other features provided by the various committees without missing that portion of the scientific program in which they were interested.

The conference on Biology of Cancer was especially interesting. Professor William T. Bovie, of Harvard University, spoke on "The Relationship Between Physiological, Dominant and Biological Effects of Rays." Dr. M. T. Burrows, from Washington University, St. Louis, spoke on the subject, "Is Cancer a True Disease or Merely the Result of a Condition of Change in the Organism?" This paper was discussed by Dr. E. C. Ernst from the radiological standpoint.

Other members contributing to the program were Drs. J. D. Southard, Fort Smith, Arkansas; W. E. Costolow, Los Angeles, California; R. H. Millwee, Dallas, Texas; J. T. Stevens, Montclair, New Jersey; G. W. Grier, Pittsburgh, Pennsylvania; J. F. Percy, Los Angeles, California; A. J. Pacini, Chicago; F. D. Dickinson, Tampa, Florida; F. D. Dickson, Kansas City; Charles G. Sutherland, Rochester, Minnesota; C. C. Dennie, Kansas City; Henry Schmitz, Chicago; Samuel B. Childs, Denver, Colorado; Adolph Hartung, Chicago; E. H. Kessler, St. Louis; F. J. Taussig, St. Louis; William Neill, Jr., Baltimore, Maryland; C. F. Burnam, Baltimore, Maryland; D. T. Quigley, Omaha, Nebraska; Sanford Withers, Denver, Colorado; W. F. Braasch, Rochester, Minnesota; Lewis Gregory Cole, New York City; J. H. Dempster, Detroit, Michigan, and Harold Swanberg, Quincy, Illinois.

A very important contribution in the conference on Light Therapy was delivered by Dr. Axel Reyn, who is physician-in-chief of the Finsen Medical Institute of Copenhagen, Denmark. Considerable interest in what seems to be the revival of the use of the carbon arc light in therapy was indicated by the approval manifested by the members on this subject following the presentation.

Thursday evening the annual banquet was held at the Muehlbach Hotel. The convocation exercises were conducted by the President in the banquet hall. The honorary degree of the Society was conferred upon Dr. Axel Reyn, of Copenhagen, Denmark, and Dr. James F. Ewing, of New York City. Two members were awarded the Society's gold medal: Dr. Preston M.

Hickey, of Ann Arbor, and Dr. Benjamin H. Orndoff, of Chicago.

Short addresses were given by Dr. Axel Reyn and Dr. E. W. Rowe. The newly elected officers were introduced and after a few short speeches and some good stories the President adjourned the meeting. Entertainment and dancing provided by the local committees were thoroughly enjoyed by the members and guests present for the rest of the evening.

The location of the exhibits relative to the scientific assembly room was convenient, and conserved greatly the time of the members who wished to visit the exhibits between periods of interest in the assembly room. The thanks of the Society are due to the exhibitors for the unusual amount of effort and expense entailed in exhibiting their lines of new equipment.

The local committees under the supervision of the general chairman, Dr. E. H. Skinner, conducted their part of the meeting in such an admirable manner as to deserve the gratitude of everyone in attendance. The ladies were provided shopping tours, automobile rides and many other social diversions during the period of the meeting.

One of the markedly pleasant features in connection with this annual meeting, to those who were enabled to participate in it, was the trip on the Radiological Special train, from Chicago to Kansas City, so admirably arranged by Dr. I. S. Trostler. A club breakfast and dinner were served on this train,—truly delightful occasions, and constituting real reasons for "going on the Special."

The Kansas City meeting appears to mark an epoch in the history of radiological organization. The character of the program construction introduced by President Stevens seems to supplant the demand for division of the assembly into sections.

The tremendous amount of influence for the good of the science of radiology in general, emanating from a well-organized society of this size, can scarcely be overestimated. It is fortunate that the new President, Dr. Arthur W. Erskine, and the President-elect, Dr. Manly J. Sandborn, are men who possess records of long experience and ability in the management of such organization work, and the members have every reason to anticipate that the same rate of progress will be maintained in the organization and that the spirit of democracy, good-fellowship and co-operation that has characterized this organization in the past will continue to the glory of the science of radiology in North America.

BENJAMIN H. ORNDOFF, M.D.

ABSTRACTS OF CURRENT LITERATURE

INDEX TO ABSTRACTS IN THIS ISSUE

Study of the infant stomach.—Owing to a scarcity of literature and a divergence of opinion on the examination of the infant stomach by the roentgen ray, the writer's work was undertaken for the purpose of studying the various functions of the infant stomach. Fluoroscopic examinations and roentgenograms were made at regular intervals before and after meals, with observations concerning form, size, position, air bubble, peristalsis and emptying time.

Three types of feeding were used with each child: (1) a milk of average caloric value; (2) a concentrated milk; (3) a gruel or mush of thick consistency. No contrast mediums were used.

1. A gruel or cereal made of milk, no matter how thick it is before ingestion, becomes fluid in the stomach under the influence of the saliva and body heat, whereas a food of mashed potatoes or vegetable mush retains its consistency.

2. The empty stomach is difficult to see with the fluoroscope. The filled stomach is clearly visible without contrast mediums and lies in the upper left quadrant of the abdomen, close to the diaphragm, extending in a horizontal plane to or just beyond the midline.

3. The stomach shadow on the plate may be defined by an upper, deeply shaded portion (the air bubble), and a lower, less intensely shaded area (the contents).

4. The air bubble varies in size, shape and form in all stomachs with fluid contents, but is distinctly smaller, or often absent, when thick gruels are swallowed.

5. There are two main, consistent types of stomach with fluid feedings, in the infant. Both are horizontal and extend to or just beyond the vertebral column to the right. *Type 1:*

The shape is that of a pear or a flask lying on its side, with a large, circular, expanded fundus and a smaller, narrow, pyloric area. *Type 2:* Occurs less frequently and is smooth, elliptical or oval in shape.

The above two types may assume a third form, common to both, when thick gruels are ingested, namely, a small, circular or oval form, about one-third the size of the fluid form, with little or no air bubble at all.

L. R. SANTE, M.D.

Roentgen-ray Studies of Stomach Function. Julian L. Rogatz. Am. Jour. Dis. Child., July, 1924, p. 53.

Effect of irradiation upon lymphatic leukemia.—Irradiation by roentgen rays and radium is a form of therapy that often brings relief to patients with chronic leukemia, though it does not cure either the lymphatic or myelogenous form. It produces distinctly more benefit in myelogenous than in lymphatic leukemia. In a previous report the author has shown from a study of 78 irradiated and 52 non-irradiated cases of chronic myelogenous leukemia that, though a very high percentage of the irradiated cases were distinctly and often very markedly benefited, the duration of life was but little prolonged.

The present report is based on a study of 98 cases of chronic lymphatic leukemia and 57 of the acute form of the disease. End-results have been studied in 80 cases of chronic lymphatic leukemia. Fifty of these had been treated by intensive irradiation from radium or roentgen rays and 30 cases received no irradiation. These latter served as a control group.

1. The decade of life in which the most cases of chronic lymphatic leukemia occur is 45 to 55. Acute lymphatic leukemia seldom occurs after the age of 25.

2. Both chronic and acute lymphatic leukemia affect males about three times as often as females. Both forms of the disease are relatively more frequent in females in the earlier than in the subsequent years of life.

3. The correct diagnosis of the chronic cases was not established on the average until 1.4 years after the first symptoms, though on the average a physician was consulted 0.55 year earlier. On the average the nature of the acute cases was not recognized by their physician until the disease had run two-thirds of its course.

4. Irradiation had no detectable effect on prolonging the duration of either form of the disease. The average duration of life, after the first symptom, of 80 chronic cases, over 30 years of age, was 3.45 years, being essentially the same for the 50 irradiated cases and the 30 that were not.

The chronic disease lasts a shorter time in younger than in older persons. About 60 per cent of all chronic cases live one to four years, and 14 per cent six to eight years. About 50 per cent of the acute cases died in less than two months after initial symptoms.

5. The early institution of irradiation did not result, in this series, in a more favorable prognosis with respect to life extension.

6. Irradiation, properly administered, undoubtedly benefits symptomatically cases of the chronic form of lymphatic leukemia, though not to the extent that occurs in chronic myelogenous leukemia. The chances of symptomatic improvement are in fairly direct relationship with the time before death that treatment is begun.

7. The beneficial effects of irradiation in acute lymphatic leukemia are but evanescent and slight.

8. Irradiation may produce a better production of the formed elements of the marrow and lessen the activity of the formation of lymphocytic cells. The hemoglobin level, numbers of blood platelets, and character of the lymphocytes serve more importantly to adjudge the patient's condition than the number of white cells. An aleukemic blood picture may occur when patients are seriously ill.

Irradiation usually causes little or no improvement in the patient's general condition when the hemoglobin is 50 per cent or less, or when outstanding purpura with thrombopenia is present, or when there are many immature and atypical lymphocytes in the peripheral blood.

9. The effect of irradiation on decreasing the size of lymph nodes or spleen in chronic lymphatic leukemia is apt to be proportional to the amount of improvement in the patient's general sense of well-being.

10. Treatment should be guided and prognosis formulated from correlated information obtained from the patient's history and physical signs, together with complete blood examinations and basal metabolic blood examinations.

By so doing, in spite of irradiation becoming less and less effective, this therapy is of distinct value and maintains the patient's efficiency usually much better than if no irradiation is given.

11. The authors express the opinion that the new irradiation methods probably will permit greater benefits from irradiation than in the past ten years.

SOLOMON FINEMAN, M.D.

Lymphatic Leukemia: Age Incidence, Duration, and Benefit Derived from Irradiation. George B. Minot and Raphael Isaacs. Boston Med. and Surg. Jour., July 3, 1924, p. 1.

Duodenal stenosis.—Roentgenographic appearances of the duodenum differ in accordance with their origin. With pyloric insufficiency the Kerkring folds lie close to each other and are well seen. With stenosis artificially produced the folds are not so close together, and dilatation of the duodenum is not seen at all or is only moderately perceptible. With chronic stenosis the duodenum is well filled, the distal parts are considerably dilated and the Kerkring folds are partially or entirely obliterated; the duodenum has a sausage appearance and may attain the diameter of the colon.

The following are to be considered among the causes of duodenal stenoses: (1) Adhesions after laparotomy; (2) adhesions due to peritonitis, tuberculosis or from other causes; (3) tumors of the pylorus, pancreas, retroperitoneal glands, etc. The author has divided the chronic duodenal stenoses into two classes: (1) Persistent stenosis, and (2) Intermittent stenosis.

In persistent stenosis the contrast material trickles constantly through the duodeno-jejunal junction, but only in a thin jet; the duodenum is completely filled because of the constant supply from the antrum. More or less violent antiperistalsis of the lower section of the duodenum may drive the food back into the bulbus and even into the stomach. The evacuation of the stomach may be delayed six to twenty-four hours. In the enlarged sac-like horizontal portion of the duodenum there may be perceived after six to twelve hours the flake-like remainder of the contrast food.

In the intermittent duodenal stenoses which are found mostly in connection with intensified peristalsis of the stomach, the contrast material fills the duodenum completely to the duodeno-jejunal junction, and stops there, as if at an absolute obstacle. There is at the same time a strong anti-peristaltic action of the horizontal and descending portions of the duodenum which drives the food back into the bulb and even into the stomach. Renewed antrum peristalsis again fills the duodenum and the play of this "pendulum movement" may continue for two to twenty minutes. The duodeno-jejunal junction then suddenly opens and the contrast food pours in a thick jet into the jejunum. The stomach evacuates well if after a quarter or half an hour's time there is no repetition of the stenosis, but with a long persisting or rapid repetition of the constriction the evacuation of the stomach is delayed several hours, which may finally result in considerable secondary ectasia of the stomach. It is evident that there may be different causes of intermittent stenosis, as a movable tumor, which, because of its location, could produce intermittent obstruction at the flexura, and traction on the mesentery resulting from the abnormal position of the stomach and small intestines in cases of marked emaciation.

J. D. CAMP, M.D.

Chronic Stenosis of the Duodenum. N. Ratkoczi. Am. Jour. Roentgenol. and Rad. Ther., Sept., 1924, p. 246.

Surgical significance of a persistent ascending mesocolon.—The author believes that a persistent ascending mesocolon in man is incompatible with perfect visceral function. Some surgeons have assumed that the ascending colon is normally considerably mobile, but they overlook the fact that they are not observing normal individuals. Their testimony, however, is significant because it shows how often mobility of the ascending colon accompanies the indications for exploratory laparotomy.

The anatomical test of motility is the presence of the ascending mesocolon in whole or in part. The radiographer has often come to the same conclusion as the surgeon—if the patient has no marked colonic stasis and no obvious colonic symptoms, he regards the picture of the ascending colon as normal. Hence the opinion that there are as many variations in the features of the normal colon as in those of the face. Here again, however, the patient is being radiated because there is something wrong with him.

In this study the author found that in 70 per cent of the cases examined in the dissecting and postmortem rooms the ascending colon did not possess a mesentery. However, in 70 per cent of those examined in the operating room the ascending colon persisted.

The writer's conception of the normal ascending colon as seen under the radiographic screen is that it is practically straight; the diameter of the cecum is but slightly greater than that of the succeeding segment of gut. There is no lateral mobility, and the ileocecal junction does not descend into the true pelvis when the patient is erect. There is always an upward excursion of the hepatic flexure of not less than two inches when the patient passes from the erect to the recumbent posture. The persistence of a mesocolon, with the consequent mobility of the ascending colon, is a congenital defect as much as the persistence of a patent funicular process or a patent urachus. It has as much relation to visceroptosis as a sore throat to diphtheria. The visceroptotic patient always has a loose ascending colon, but the majority of patients with a loose ascending colon do not have visceroptosis, nor any of its stigmata. The unfixed descending colon is just as frequently found in men, and just as frequently produces symptoms in men as in women. The ascending

colon, by virtue of a persistent mesocolon, can become twisted, obstructed, or displaced.

The factors which keep the ascending colon in its normal position are: (1) the fact that it lies on an inclined plane; (2) the postural tone of the anterior abdominal wall; (3) the fact that it has lateral attachments, lying as it does behind the parietal peritoneum. These simply prevent the colon from migrating towards the middle line, without which migration it cannot prolapse into the true pelvis. The psoas muscle forms a prominent ridge medial to the ascending colon, and the latter cannot descend unless it gets over this ridge.

When a complete mesentery is present the only factor missing is the lateral attachment, and whether it is the abdominal muscles that displace it or not, there is no shadow of doubt that when the patient assumes the erect posture, the ascending colon often passes medially and prolapses, so that the cecum lies in the bottom of the true pelvis. This the author calls the prolapsed type. He has seen it in individuals with the abdominal walls of prize-fighters. If the cecum is in the true pelvis, contraction of the abdominal wall alone only presses it farther towards the hollow of the sacrum and cannot restore it to the right iliac fossa.

In some instances the cecum may be wedged in between the tonic abdominal wall and the floor of the right iliac fossa, or a strong parietocolic fold may fix the gut just above the cecum, so that the unfixed hepatic flexure falls down in front of it or to the side of the proximal part of the ascending colon, constituting the angulated type of ascending colon. This type is frequently associated with symptoms of subacute obstruction. The angulation is present only when the patient is standing up; the obstruction is present only when the colon attempts to evacuate its contents,—hence the dependence of symptoms on posture and the ingestion of food.

The hepatic flexure is connected to the second stage of the duodenum by peritoneum. When the unfixed ascending colon is displaced downwards, the second stage of the duodenum also descends downwards, the distance depending upon the degree of fixation of the first stage of the duodenum. If this portion is highly placed and fixed, it becomes angulated by tension on the second stage. If the first stage is mobile, the drag on the second stage draws the whole supramesocolic portion downwards and forwards, and a kink occurs below the point of attachment of the transverse mesocolon.

The author believes that pain in gastric ulcer is often due to gastric distention, which is frequently associated with obstruction of the duodenum, resulting from a mobile hepatic flexure. A recumbent posture in such cases frequently relieves both the pain and the vomiting. Radioscopy usually reveals a six-hour gastric retention, with a tenderness over the first stage of the duodenum. At operation the duodenum appears normal till the mobile hepatic flexure is drawn downwards, and immediately the kinking of the duodenum is apparent.

The work of Bloodgood, Stavely, Kellogg, and Wilkie has placed the condition known as arterial duodenal ileus on a sound basis. The author has observed 38 cases. In 37 of these the ascending colon possessed a complete mesentery. X-ray examination in 36 cases showed that the cecum lay in the true pelvis when the patient was erect. None of these cases had general visceroptosis. It is the writer's belief that relief from pain following the assumption of a doubled up or squatting posture is a pathognomonic sign of duodenal ileus.

In conclusion, the author is aware of the fact that many individuals with mobile cecums never have an abdominal symptom in their lives, that many get their first symptom after the age of thirty, and that many have long periods of immunity between attacks. All he claims is, that a mobile colon is a predisposing factor in the causation of certain abdominal complaints.

SOLOMON FINEMAN, M.D.

The Surgical Significance of the Ascending Mesocolon. A. A. McConnell. Irish Jour. of Med. Sci., Sept., 1924, p. 402.

Inverse square of distance law.—The authors report a series of experiments undertaken to prove the accuracy of the inverse square of distance law for filtered roentgen radiation. The determinations were made by iontoquantimeter measurements and clinical experiments.

The results of ionization (iontoquantimeter) experiments, with thicknesses of aluminum ranging from 0.25 to 3 mm., conformed approximately to the inverse square of the distance law. Carefully conducted skin tests gave results which supported those obtained with the iontoquantimeter. The authors conclude that the law for filtered radiation is the same as that for unfiltered radiation and that the intensity varies inversely as the square of the distance and not inversely as the distance.

J. D. CAMP, M.D.

Inverse Square of Distance Law for Filtered Roentgen Radiation. George M. MacKee and George C. Andrews. Am. Jour. Roentgenol. and Rad. Ther., July, 1924, p. 58.

Duodenal and gastric ulcer.—Surgical treatment of gastric and duodenal ulcer is still a matter of controversy both as to operative indications and the best method of procedure. The author feels that chronic duodenal ulcers should be treated first medically and if improvement occurs and the patient understands the condition and dangers he feels that no other treatment is necessary. Even acute duodenal ulcers should first receive a thorough course of medical treatment; surgery should be reserved for those cases that do not respond. The author does not agree with views recently set forth that large resections of the pylorus should be made in attempting to eradicate duodenal ulcers. His belief is that simple gastro-enterostomy, properly performed, is curative and adequate in a great majority of chronic duodenal ulcers; that from 80 to 90 per cent of the patients so treated are completely relieved of their symptoms and cured. Gastrojejunal ulcer occurs in less than 20 per cent of all cases; malignancy occurs so rarely as to be negligible.

A detailed description is given for operative procedure when the ulcer is located at various sites.

Chronic gastric ulcers present problems differing radically from chronic duodenal ulcers. Eradication of the ulcer is essential. Local excision with cautery destruction and gastro-enterostomy is the method of choice.

L. R. SANTE, M.D.

The Present Status of the Surgical Treatment of Chronic Duodenal and Gastric Ulcer. Charles H. Peck. Ann. Surg., July, 1924, p. 31.

Radiation of tonsils and other areas of lymphoid tissue.—Much that is written on radiation of the tonsil is bewildering. For example, Barnes admits that undoubtedly a complete and lasting atrophy of the tonsil might result through radiation, but damns the treatment by faint praise by recommending only the split capsule operation, and adds that "radiation can be given with safety and no untoward results, and should be given a trial in some cases."

The author summarizes the work of several men, emphasizing the importance of other areas of lymphoid tissue in the throat which are not touched by operation but are affected by X-ray. He summarizes: (1) the tonsils and adenoids are only a part of the diseased lymphoid tissue in the average infected throat; (2) small repeated doses of X-ray, 1/20 to 1/5 of a skin unit at two weeks' interval, will cause any degree of atrophy of lymphoid tissue without damaging other tissue; (3) a biochemic change takes place which inhibits bacterial growth; (4) X-ray will cause shrinkage, recovery of protective epithelium, and immunity.

W. W. WATKINS, M.D.

X-ray Treatment of Tonsillar and Associated Lymphoid Tissue. C. A. Rutherford. Northwest Med., June, 1924, p. 258.

Tonsillar infection.—(NOTE: The above abstract represents the sanguine viewpoint of many radiologists, while the following abstract represents that of many laryngologists. They present the two extreme views.)

This author bases his conclusions regarding the inefficiency of radiation of tonsils on the claims that this method does not dispose of the infection, nor reduce the tonsils in size, quoting in support of this the reports of Nuzum, Lederer, Borden, Babcock and Shurley.

From these data he claims that we must be skeptical as to the value of roentgen rays in ridding the tonsils of bacteria, and must not be attracted away from the only adequate measure of removing diseased tonsils. In some cases, it may be justifiable to delay surgical intervention while radiation is being tried; in other cases delay would be disastrous.

W. W. WATKINS, M.D.

The Present Status of Roentgen-ray Therapy for Diseased Tonsils. O. M. Rott. Northwest Med., June, 1924, p. 260.

Salpingitis complicating uterine cancer.—A report based on a study of 404 cases of cancer of the uterus treated by radiation, among which there occurred five times a severe peritonitis, which resulted in the death of four and the recovery of one. The authors conclude that chronic salpingitis complicating uterine cancer may prove disastrous and may produce peritonitis and death following radiation. However, they do not believe that all cases of gonococcic infection complicating cancer of the uterus will cause such severe and disastrous results. The intra-uterine manipulation may be a factor in the lighting up of old gonococcic infections, but it was not the sole cause in the cases reported, and external radiation alone in cancer doses may light up a gonococcic salpingitis.

J. D. CAMP, M.D.

Untoward Results in Radiation Therapy of Uterine Cancer When Complicated with Latent Gonococcic Salpingitis. B. F. Schreiner and L. C. Kress. Am. Jour. Roentgenol. and Rad. Ther., July, 1924, p. 51.

Treatment of cancer of the lip.—This is a report of 136 cases of cancer of the lip irradiated at the Buffalo State Institute for the Study of Malignant Disease. The observations cover a period of eight years (1915-1922). This series does not include basal cell epitheliomata, but only the prickle cell and mucous membrane epitheliomata.

A detailed classification of cases into groups and types of tumor, and the technic used are given in the paper. The authors' conclusions are:

1. By classifying cancer of the lip into groups, the probable outcome of the treatment can be determined in the great majority of the cases and more definite results can be obtained.
2. They have demonstrated that epithelioma of the lip has been healed and remained healed over a more or less extended period of time by treatment with unfiltered X-rays.
3. Cases which have an involvement of the lymphatics, but from the standpoint of surgery are considered in an operable stage, can be healed in at least 34 per cent of cases by X-ray therapy alone.
4. Cases in which there is extensive involvement of the lymphatics, periosteum of the mandible, and ulceration, should not be treated by irradiation with any expectation of a cure.

SOLOMON FINEMAN, M.D.

Contribution to the Treatment of Cancer of the Lip by Irradiation. Bernard F. Schreiner and Louis C. Kress. Jour. of Cancer Res., July, 1924, p. 221.

The cecocolic sphincteric area.—A certain portion of the colon just distal to the caput coli, known as the cecocolic sphincteric tract, has a significance in the human which has not been appreciated until now. Roentgen-ray studies, however, would indicate that this tract functionates to a greater or less degree in human beings as it does in herbivorous animals, and that it must be taken into consideration in studies of the caput coli.

The manner of control over this tract is not known; normally it appears to be in a state of contraction, but it is not under the control of the sympathetic splanchnic nerves which control the ileal sphincter. It is subject to numerous reflex influences.

Almost all lesions of the ascending colon are most frequently found in the cecocolic tract, which may be explained by several reasons: (1) it is a vestigial structure; (2) like all points of luminal narrowing, it is quite vulnerable to disease; (3) it is a region of great functional activity.

Spasm of the cecocolic area is a common phenomenon, and may be due to disease in the area itself, to presence of irritating contents in ileum or cecum, to disease of the terminal ileum, appendix, cecum or the cecocolon, to ulcer or tumor of other portions of the colon, to ulcer of the duodenum or functional conditions in the stomach, as a part of a general or local vagotonia. A spastic contraction of the cecocolic sphincteric area can be demonstrated roentgenologically and its presence should have an important significance in the investigation of the abdomen for disease of the gastro-intestinal tract.

W. W. WATKINS, M.D.

The Cecocolic Sphincteric Tract. I. Seth Hirsch. Med. Jour. and Rec., June 4, 1924, p. 541.

Pneumothorax.—Attention has thus been called to the frequency of spontaneous pneumothorax. This accident occurred six times in a group of 43 initial cases during a period of ten months. The etiology is obscure in cases with a large pleural space, especially when the accident occurs only a few hours after the initial collapse. The rupture of marginal emphysematous blebs is a strong possibility. Whether these blebs can be recognized on the X-ray plate is a problem worthy of the attention of roentgenologists. It seems that a slight change in the negativity of the intrathoracic pressure is as potent a factor as very high pressures in tearing up adhesions. Sudden onset of pain shortly after a gas refill, coincident with a rise in fever, and the partial or total relief from the acute symptoms after the appearance of an effusion, should be considered at least suspicious evidence of a spontaneous pneumothorax. Sharp pain alone, without fever or a subsequent effusion, does not exclude the possibility of a spontaneous pneumothorax from the accidental or intentional introduction of a needle into the lung, even in the apparent absence of a free pleural space. Valvular pneumothoraces require the introduction of a rubber catheter into the pleural cavity for continuous aspiration of air. There is practically no danger of pleural infection from such a procedure. When free drainage of air fails to relieve the circulatory symptoms, digitalis in large doses is indicated. In case an empyema develops, repeated aspirations with or without replacement of air should be persistently tried before resorting to rib resection and open drainage.

L. R. SANTE, M.D.

Spontaneous Pneumothorax during the Course of Artificial Pneumothorax. I. D. Bronfin. Am. Review of Tuberculosis, June, 1924, p. 346.

Leukemia.—Of the twenty-five cases, 16 were of the lymphatic type and 9 of the myelogenous variety. The average duration of the lymphatic type was one year and seven months, and in the myelogenous type two years and three months. Due to the fact that a remission is often induced with the least degree of discomfort to the patient and in a short time, the authors believe that the roentgen ray and radium are destined to hold a leading place in the treatment of this disease.

Early cases were treated with 90 KV., 4 mm. Al. filter, and a short target distance, over the spleen, glands and long bones. More recently the radium pack giving 15,000–16,000 mc.-hr. filtered through 2 mm. brass and 1 mm. Al. was used. In cases treated with deep roentgen therapy, 200 KV., copper filtration, long target distance and 8 ma., the response was equally encouraging.

While being enthusiastic with the results of short wave therapy in securing remissions with the least discomfort to the patient, the authors lay stress on the fact that in their experience the remissions have not been permanent and that the ultimate fate of the patients is the same.

J. D. Camp, M.D.

Radiation Therapy in Treatment of Leukemias, Summarized from a Series of Twenty-five Cases. B. F. Schreiner and W. L. Mattick. Am. Jour. Roentgenol. and Rad. Ther., Aug., 1924, p. 126.

Laryngeal injury induced by X-ray treatment.—The author reports a case of lymphoma of the front of the neck, in which hoarseness appeared in the course of X-ray treatment. The treatment was repeated and eight months later the patient developed pain in the throat, and dyspnea. The skin in front of the neck became markedly atrophied, with a great dilatation of the vessels. Ulceration, fistula, and sequestrum formation of the thyroid cartilage followed. The patient finally recovered, but his voice remained hoarse and the mucous membrane of the larynx remained swollen.

The author cites conclusions from the papers by Marschick and Jüngling to the effect that the earlier X-ray reactions take place in the skin and the subcutaneous tissues or in the submucosa, while the late reaction is found in the muscles, perichondrium, and glands, where most serious degenerative processes may be found. Degeneration of the muscles of the neck and the larynx, as well as perichondritis, may develop, and the cartilage of the larynx may be destroyed, forming sequestra with deep unclean ulceration.

Infiltration and edema may also be found, and the patient becomes hoarse, with pain and difficulty in breathing and swallowing, and very often it becomes necessary to perform tracheotomy and gastrostomy. Tracheotomy is very difficult on account of the condensation of the tissues of the neck induced by the X-ray reactions in the skin and muscles; laryngectomy is absolutely impossible because the operative wound cannot heal when the skin and muscles have been subjected to X-ray alterations. It is of importance to note that the late reaction need not be preceded by other reactions.

According to Marschick, Hoffmeister, and Jüngling the prognosis of the late reaction cases is bad, if sequestration has taken place; nearly all the patients died. Jüngling is of the opinion that no operable cases of laryngeal cancer should be treated by X-rays.

Solomon Fineman, M.D.

Injury to the Larynx Induced by X-ray Treatment. Ove Strandberg. Jour. Laryngol. and Otol., Aug., 1924, p. 437.

Blood changes due to irradiation.—A considerable portion of this article is devoted to a review of the literature, as found in some 78 articles listed in the bibliography. Original investigations reported had in mind the determination of the degree and duration of changes in white cell count produced by therapeutic doses of short wave length rays, as contrasted with longer wave length rays, in patients not suffering from any disease of the blood-forming organs. Observations were made on 42 patients with various forms of malignant disease. The first group, of 20 patients, were studied before and after receiving one course of treatment of comparatively long wave lengths. The other 22 patients were studied before and after receiving short wave length treatments, varying from 338 to 1,950 m.a.m., at 220 KV., 31 in. distance, ½ mm. copper filter.

As found by other observers, both long waves and short waves first produce a transient leukocytosis, followed by leukopenia and lymphopenia. The leukocytosis is due to increment of polymorphonuclear neutrophiles, the lymphocytes being reduced from the start except when very small doses are given, when a lymphocytosis may result.

The fall in lymphocytes is greatest in the first twenty-four hours, while the white count reaches its lowest point in about six days, when short wave lengths are used. An eosinophilia is usual two or three weeks after short wave length irradiation. The blood contains many degenerated white cells in the first three days after irradiation, and there is a slight increase in platelets. Important changes in hemoglobin and red cells do not occur. The clinical condition of the pa-

tient may influence the treatment, but anemia *per se* does not seem to be of great importance. The amount of radiation and the surface area irradiated are both of great importance in determining the degree and duration of effect on the white cells. Prior to irradiation, the blood should be examined, and after one dose has been given, before another is administered, blood examination should be made. If leukopenia (count below 5,000 per c.mm.) is present, repetition of treatment may become a serious event.

W. W. WATKINS, M.D.

The Effect on the Blood of Irradiation, Especially Short Wave Length Roentgen-ray Therapy. George R. Minot and Roy G. Spurling. Am. Jour. Med. Sci., Aug., 1924, p. 215.

Radiotherapy for uterine conditions.—On the basis of cases taken from their files, these authors report on the treatment of the following: Essential hemorrhage of the adolescent, essential hemorrhage in the childbearing period, post-operative uterine hemorrhage, hemorrhage of the menopause or uterine fibrosis, uterine fibroids, uterine fibroids after menopause, dysmenorrhea, endocervicitis.

Four cases of essential hemorrhage of the adolescent have been treated with radium, the dosage varying from 42 to 400 mgh. All were relieved, normal menstruation being resumed in from four to six weeks.

Seven cases of essential hemorrhage in the childbearing period were treated, one case requiring a second dose. Dosage was from 125 to 925 mgh. All these cases are free of symptoms and have been discharged as cures.

Ten cases of post-operative uterine hemorrhage. following removal of one or both tubes and the greater portion of both ovaries. Six cases were given X-ray only as pelvic infection existed, one had X-ray and radium, and the other three radium only. All of these cases have been traced and all have been in excellent health for more than a year.

Seventeen cases of hemorrhage of the menopause period were without detectable pelvic pathology. Nine received radium only, four X-ray and radium, and four X-ray only.

Sixty-one cases of uterine fibroids have been treated, twelve of them with fibroids larger than a four months' pregnancy.

Twelve cases of dysmenorrhea, in ten of whom a permanent menopause was desired, and excellent results are recorded in all. Either X-ray or radium will give satisfactory results.

Two cases of endocervicitis were treated satisfactorily.

The authors state that it will soon be recognized that fibroids may be removed by radium, X-ray or abdominal hysterectomy, and it only remains to select the safer and easier method for the patient.

W. W. WATKINS, M.D.

Radiation in Benign Affection of the Uterus, with a Report of Cases. D. Y. Keith and J. P. Keith. Ken. Med. Jour., July, 1924, p. 264.

Lower back pain.—Twenty consecutive cases showing calcification of the ilio-lumbar ligaments are recorded. Fourteen were in females and 6 in males. Fourteen complained of back pain, 2 of neuritis, 2 of rheumatism, and 2 of symptoms referable to the urinary tract. In 12 of the cases, the roentgenograms showed definite evidence of infectious arthritis involving the lumbar spine or sacro-iliac joints.

J. D. CAMP, M.D.

The Rôle of Ligamentous Calcification in Lower Back Pain. H. P. Doub. Am. Jour. Roentgenol. and Rad. Ther., Aug., 1924, p. 168.

Radium technic for lesions on lip.—Some cases are very difficult to handle with X-ray, and in one case reported by this author, radium was effective when X-ray had failed. X-ray produced the desired epilation but only temporary relief. Condition had existed six years, and was associated with a rhinitis; lesions were on the upper lip. A rectangular applicator was used, screened by 0.3 mm. brass shield, and the whole enclosed in rubber dam. This was a half-strength applicator and was allowed to remain in position five and a half hours. Uniformity in firmness of apposition is essential. Patient has been free of symptoms for two and a half years.

W. W. WATKINS, M.D.

Sycosis Vulgaris and Radium. R. R. DuCasse. Ohio St. Med. Jour., June, 1924, p. 357.

Radium therapy in eye and throat conditions.—At the Boston City Hospital, there was established in August, 1922, a clinic for radium treatment of eye, ear, nose and throat conditions. One conspicuous feature of the work done there during the past year is that 98 per cent of the conditions treated were non-malignant.

Cases in which tonsillectomy was not desired have been treated with radium, three methods being tried,—namely, radium held against the oral side of the tonsil, applied externally at 2 cm. distance and screened with brass and rubber, and by plunging needles into the body of the tonsil. It was found that fifty milligrams buried in the tonsils for from fifteen minutes to

one hour and repeated at weekly intervals, gave the best results. Radium converts the tonsils into small, firm, fibrous lumps of tissue.

Quite a little work has been done on corneal scars and cataracts. One congenital and two incipient senile cataracts have shown marked improvement. Four cases of corneal scars have shown definite improvement.

W. W. WATKINS, M.D.

Radium Clinic for Treatment of Eye, Ear, Nose and Throat Conditions. J. J. Corbett. Boston Med. and Surg. Jour., June 19, 1924, p. 1082.

Glaucoma.—Continuing the report of work done at the Boston City Hospital clinic the writer reports what he considers one of the most spectacular results from radium, namely, the relief of glaucoma.

Three cases are reported in some detail, in all of which the intra-ocular tension was promptly reduced by radium, and this was offered as a very efficient pre-operative method in place of paracentesis of the cornea or sclerotomy preceding the operation for glaucoma.

W. W. WATKINS, M.D.

Effect of Radium on Glaucoma. J. J. Corbett. Boston Med. and Surg. Jour., June 26, 1924, p. 1124.

Endocrine cases.—Growth defects of endocrine origin can be grouped under one or more of the following heads, based on the evidence furnished by the roentgen ray: (1) Retardation, (a) retarded bone growth, (b) delayed maturation as shown by closure of the epiphyses; (2) acceleration, (a) rapid bone growth, (b) premature epiphyseal closure or synostosis of the sutures. Retardation in the time of appearance of bone nuclei and in the skeletal growth is noted in: Hypopituitarism, hyperthyroidism, and infantilism. Delay in epiphyseal closure is noted in: Hypothyroidism, hypopituitarism and eunuchoidism. Accelerated bone development is observed in: Eunuchoidism, hyperpituitarism, and precocious puberty. Premature closure of the epiphyses or sutures is observed in: Precocious puberty and hyperpituitarism.

In reviewing the cases the author found that the majority of endocrine conditions present no single outstanding characteristic or group of characteristics which makes diagnosis possible by roentgen means alone. The clear-cut case of acromegaly is the only exception. According to the author the roentgen examination of the feeble-minded shows (a) a very high percentage of malformations and developmental defects of the skull; (b) in those cases associated with endocrine disturbances there are, as well, marked changes in the process of bone development; (c) recognizable changes in the bony structure of the sella turcica are relatively uncommon, even in those conditions in which the pituitary gland is involved.

J. D. CAMP, M.D.

Roentgen-ray Studies of the Feeble-minded. M. W. Clift. Am. Jour. Roentgenol. and Rad. Ther., July, 1924, p. 23.

Blastomycosis.—In 1894 Gilchrist described before the American Dermatological Society, a yeast-like organism which he found in a section taken from a patient with an unusual dermatitis. He classified the organisms as blastomycetes and named the disease blastomycetic dermatitis. Later these organisms were described in internal organs and the disease was termed saccharomycosis hominis. The bacteriological and clinical features of these two cases were quite identical with those subsequently reported by various men as blastomycosis or oidiomycosis.

The detailed history of a case of this type is given, starting with an infection following a mashed finger, developing large abscess and cauliflower-like growths throughout the body. Under 150 grains of K. I. daily these heal rapidly. Large doses of X-ray should not increase in rapidity of healing. Cultural characteristics are given in detail.

L. R. SANTE, M.D.

Systemic Blastomycosis (Oidiomycosis). Warren H. Cole. Ann. Surg., July, 1924, p. 124.

Application of radium to tonsils.—The author describes the instruments devised by him for application of radium to the tonsils, and the technic of application. Radium is in a small chamber, the rays emerging through a window on one side, and in this window various thicknesses of filter may be used. A usual treatment is with 38 mg. radium element and filter of .58 mm. aluminum, and ten-minute application, the window being held in contact with the tonsil. Subsequent treatments may be longer (15 or 20 minutes), and are given at intervals of three or four weeks, the average number being four treatments.

This paper reports 101 cases of faucial and four cases of lingual tonsils.

Ten patients with enlarged tonsils all had varying reduction in size of tonsils. In 26 cases of tonsillitis, the size of tonsils was reduced in all. In 17 cases of arthritis, associated with tonsillitis, there was improvement in all. In 14

cases of arthritis, the symptoms diminished or disappeared in all. In 21 cases with miscellaneous conditions, satisfactory results were obtained. There were 13 patients who had had previous tonsil operations.

Three of the patients who had radium treatment had tonsillectomy after this treatment; in one the tonsils were large and fibrous; in the second there was an uncomfortable sensation in the throat although tonsils were reduced in size; in the third an acute attack before radium treatment was completed led the patient to have a tonsillectomy.

In this author's experience of three years, radium has advantages in cases that are not good operative risks; where tonsillectomy has been incomplete; where diagnosis is obscure. In how large a proportion of cases where tonsillectomy is ordinarily advised, radium should be used, time and further experience will demonstrate.

W. W. Watkins, M.D.

The Use of Radium Radiations in the Treatment of Tonsils: A Further Report. Francis H. Williams. Am. Jour. Med. Sci., July, 1924, p. 18.

Chloride metabolism in roentgen-ray therapy.—Cori and Pucher found that roentgen radiation produces a definite chloride retention, more marked when sickness occurs. Schlagintweit and Sielmann state that in severe disturbances following large doses of X-rays there is a decrease in the chloride content of the blood and that sodium chloride administered in any form gives full relief.

The authors have studied twelve cases. The data obtained are not as yet regarded as sufficient to permit definite statements, but are sufficient to warrant the following tentative conclusions:

1. Roentgen-ray therapy in massive doses produces a definite lowering of urine excretion (confirmation of Dodds and Webster), and a chloride retention (confirmation of Cori and Pucher) when the upper abdomen is radiated. Radiation of other parts of the body produces less effect.

2. With radiation of the upper abdomen, where the previous chloride excretion is low, the tendency to sickness, other things being equal, is greater.

3. Preliminary feeding of sodium chloride daily, so that the chloride excretion is raised to ten or more grams per day before treatment is commenced, with continued administration during treatment, prevents or lessens the sickness.

4. The blood chloride is not invariably affected, though sometimes the percentage is lowered.

Solomon Fineman, M.D.

Chloride Metabolism in Roentgen-ray Therapy. A. T. Cameron and J. C. McMillan. Lancet, Aug. 23, 1924, p. 365.

Back pains, chronic and acute.—Mechanically the lumbosacral and sacro-iliac regions are weak spots. The relaxation of ligaments is primarily the cause of a large majority of acute and chronic back pains; infection, toxemia, combined with the anatomical variations in this region, are responsible for acute back pains. Spondylolisthesis is a result of improper bony contact at the articulations or a loss of bone continuity in the neural arch of the fifth lumbar. In order to determine the cause of certain of these conditions roentgenograms should be made at various angles, taking into consideration these anomalies, before more information is obtained on this subject.

J. D. Camp, M.D.

Reasons for Lack of Positive Roentgen Findings in Many Cases of Low Back Pain. Paul B. Magnuson. Am. Jour. Roentgenol. and Rad. Ther., July, 1924, p. 15.

Arthur W. Fairbank.

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